Exhibit U

UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

IN RE: JOHNSON & JOHNSON TALCUM POWDER PRODUCTS MARKETING SALES PRACTICES AND PRODUCT LIABILITY LITIGATION	)	MDL 16-2738 (FLW)(LHG)
THIS DOCUMENT PERTAINS TO ALL CASES	)	

WEDNESDAY, DECEMBER 19, 2018

CONFIDENTIAL - PURSUANT TO PROTECTIVE ORDER

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Videotaped deposition of Laura Plunkett, Ph.D., DABT, held at the Four Seasons Hotel, 999 North 2nd Street, St. Louis, Missouri, commencing at 9:12 a.m., on the above date, before Carrie A. Campbell, Registered Diplomate Reporter, Certified Realtime Reporter, Illinois, California & Texas Certified Shorthand Reporter, Missouri & Kansas Certified Court Reporter.

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VIDEOGRAPHER:
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EXHIBITS

(Exhibits attached to the deposition.)

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VIDEOGRAPHER: We are now on the record.
My name is Jacob Arndt. I'm a videographer for Golkow Litigation Services.
Today's date is December 19, 2018, and the time is 9:12 a.m.
This deposition is being held in St. Louis, Missouri, In Re: Johnson & Johnson Products Marketing Sales Practices, for the United States District Court for the District of New Jersey.
The deponent is Dr. Laura Plunkett.
Will counsel please identify themselves?
MR. MEADOWS: Ted Meadows for plaintiffs.
MS. PARFITT: Michelle Parfitt for the plaintiffs.
MR. BEATTIE: Ryan Beattie for plaintiffs.
MR. TISI: Chris Tisi for plaintiffs.

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MR. GOLOMB: Richard Golomb for plaintiffs.
MR. LOCKE: Tom Locke for the Personal Care Products Council.
MS. TINSLEY: Caroline Tinsley for PTI Union, LLC, and PTI Royston, LLC.
MR. SULLIVAN: Ryan Sullivan for Imerys.
MS. BOCKUS: Jane Bockus for Imerys.
MR. SMITH: William Smith for Johnson & Johnson.
MS. BRANSCOME: Kimberly Branscome for Johnson & Johnson.
VIDEOGRAPHER: Thank you.
The court reporter is Carrie Campbell and will now swear in the witness.
LAURA PLUNKETT, Ph.D., DABT, of lawful age, having been first duly sworn to tell the truth, the whole truth and nothing but the truth, deposes and says on behalf of the Defendant Johnson & Johnson, as follows:

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DIRECT EXAMINATION
QUESTIONS BY MS. BRANSCOME:
Q. All right. Good morning, Dr. Plunkett. I introduced myself right before we started, but my name is Kimberly Branscome, and I am here on behalf of Johnson & Johnson.
Is it your understanding today that you are giving your deposition for the purpose of a Daubert analysis in the MDL related to Johnson's baby powder?
A. That's my understanding, yes.
(Plunkett Exhibit 1 marked for identification.)
QUESTIONS BY MS. BRANSCOME:
Q. I want to start by handing you what I will mark as Plunkett Deposition Exhibit 1.
Do you recognize the document that I just handed you?
A. Yes.
Q. Okay. Have you seen this document before?
A. Yes.
Q. All right. When was this

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document provided to you?
A. Either earlier this -- this week or late last week. I don't recall if it was Friday or Monday.
Q. Okay. For the purposes of the record, could you just identify what the document is that I just handed you as Plunkett Deposition Exhibit Number 1?
A. It's a notice of oral and videotaped deposition for myself, dated -- I don't see the date, but probably on the very last -- do you need that or just -- is that enough of an identification?
Q. That's all right.
Now, contained within the deposition notice there is a reference to a request for materials that are identified in more detail in Schedule A.
Do you see that?
A. Yes.
Q. Have you reviewed Schedule A?
A. Yes.
Q. Did you bring any documents with you in response to the request in Schedule A?

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A. The only thing that I believe that I had to bring that had not already been provided was additional billing since the time of my last deposition.
Q. Okay. And is it my understanding that the documentation related to additional billing that you have done since your prior deposition was produced yesterday at the deposition in the Forrest case?
A. That's correct.
Q. All right. And the information contained in the documents produced at the Forrest deposition yesterday, do those contain an up-to-date record of the billing that you have submitted for your work in connection with the litigation against Johnson & Johnson?
A. Yes, with the understanding that I haven't submitted a bill for December yet.
Q. Okay. How much time have you spent working in connection with your opinions in the case against Johnson & Johnson related to its baby powder in the

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month of December?
A. So I'm -- on all the cases that I am involved in that are pending, not just this deposition?
Q. I'll ask first all cases and then we'll narrow it to the deposition.
A. So in all --
Q. I mean to the MDL, I'm sorry.
A. Okay. So in all cases this month, probably eight hours so far, maybe ten.
Q. Does that include the time that you've spent attending deposition?
A. No, that's not including yesterday's deposition time. I apologize. I forgot about that.
Q. And how much of the eight to ten hours that you have spent this month working on these cases against Johnson & Johnson, setting aside the time you spent in deposition yesterday, relate to the MDL specifically?
A. So it will probably be billed -- it will be one bill for the preparation time because the prep overlapped,

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but I'll bill separately for the time I spent yesterday right before the deposition and then at the deposition, so...
Q. What did you do to prepare for your deposition today?
A. I reviewed my reports, the three reports that I filed in the litigation. I had a meeting with attorneys on Monday, and then we had a short meeting yesterday evening because some attorneys arrived that were not here on Monday.
And essentially went through some of the documents that -- went through some of the documents that I had cited in the report in certain paragraphs, just to refresh my memory of what they were. So if you want me to tell you which paragraphs, I can do that.
Q. I will in just a moment. Okay.
A. Want me to repeat that? I'm sorry.
Q. That's all right.
Dr. Plunkett, you referenced the fact that you reviewed specific paragraphs of your expert reports in

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preparation for today's deposition.
Could you identify those paragraphs for me?
And it's helpful to you, we can go ahead and mark your three expert reports, if you're referring to all three.
A. I'm going to refer just to the MDL report because that's what we're here to talk about. I mean, if you want to talk about what I did to get ready for yesterday separately or --
MR. MEADOWS: Might be helpful to go ahead and mark them.
MS. BRANSCOME: Why don't we go ahead and just mark the three reports, and then we can walk through.
(Plunkett Exhibits 2, 3 and 4 marked for identification.)
QUESTIONS BY MS. BRANSCOME:
Q. So, Dr. Plunkett, do you have a copy of your three reports in front of you?
A. Yes, I do.
Q. Do those contain any markings, highlightings or flags?
A. No, they don't.

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Q. Okay. Do you mind if we mark your copies as the official records?
A. No, that's fine.
Q. So we will mark -- well, let's do this in chronological order. So I am marking as Plunkett Deposition Exhibit Number 2 the expert report of Dr. Plunkett dated October 5, 2016.
Could you confirm, Dr. Plunkett, that that's what I marked as Deposition Exhibit Number 2?
A. Yes, it is.
Q. And then we will mark as Deposition Exhibit Number 3 supplemental expert report of Dr. Laura Plunkett dated August 29, 2018.
Dr. Plunkett, could you confirm that I marked that as Exhibit Number 3?
A. Yes, that's correct.
Q. And then Exhibit Number 4, we will mark the expert report dated November 16, 2018, by Dr. Plunkett that was produced in the MDL.
Could you confirm that I marked that as Deposition Exhibit Number 4?

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A. Yes, that's correct.
Q. All right. And so now back to the question of you referenced the fact that you looked at specific paragraphs of your expert report in preparation for today's deposition. If you could, using Deposition Exhibit Number 4, identify which paragraphs you looked at specifically in preparation for the deposition.
A. So it wasn't the paragraphs. There were certain documents in paragraphs, so that's what I was referring to, so...
So starting in paragraph 38 where I'm talking about sort of the timeline of information about human health hazards and talc dust. So I just went back and refreshed on a few of the older papers.
I looked again at the patent documents that are cited in the first bullet.
I looked again at a paper by Eberl, 1948, which is in the last bullet. The patent documents are also there as well.
And that -- so that would be all I pulled in that paragraph.
I believe that those documents

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are also cited in paragraph 39 as well, some of those same ones that are...
And then in Section 5 of my report where I'm talking about exposure, I looked again at Parmley and Woodruff. I looked again at Vetner and Iturrulde and Egli and Newton last night.
And the only other thing I looked at is not cited in this report because it came out after the report was filed, and that was -- and I did bring a copy of that. That was the risk assessment that was done in Canada. Some people refer to it as -- by the first author's last name, Taher, T-a-h-e-r. And I may be pronouncing that wrong, but...
(Plunkett Exhibit 5 marked for identification.)
QUESTIONS BY MS. BRANSCOME:
Q. All right. And I see that you brought a copy of that document with you. Just for the purposes of the record, let's mark that as Plunkett Deposition Exhibit Number 5.
Are there any markings, highlightings or notations on that document?

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A. No, there's not.
And then the other document I looked at that was not cited in the report, there is a printout from the government of Canada website that talks about some statements on talc, and so I printed that out as well. This was published at the same time that the risk assessment was published.
(Plunkett Exhibit 6 marked for identification.)
QUESTIONS BY MS. BRANSCOME:
Q. All right. We'll mark that for purposes of the record as Plunkett Deposition Exhibit Number 6. We might come back to those documents.
So returning briefly to the deposition notice and the requests in Schedule A, the billing information you produced yesterday and then we just discussed additional information with respect to that, are there any other documents that you have in your possession that are responsive to requests identified in Schedule A that have not been produced?
A. I don't believe so, no.

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Everything -- I do believe that there were some objections filed to this, so there's some things that I did not provide based on that.

Some of the things I don't have, too. I think you asked for -- maybe you didn't ask for that. Usually people ask for copies of old depositions, and I don't keep those. And maybe you didn't ask for that, but that's usually a request.

Let me see.

Q. Okay. Now, you mentioned that you met with attorneys on Monday. And who was present at that meeting?

A. So on Monday it was Mr. Meadows, sitting here. Ms. Tucker, Mr. Beattie, were at the meeting on Monday.

Q. All right. And how long did that meeting last?

A. Probably six hours, I guess, six hours with them, and then I also did some other work on my own, but...

Q. Okay. And then you mentioned that you had another meeting last night.

Who was present at that

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meeting?

A. So that was probably about an hour, and that would have been Mr. Tisi -- or maybe two hours. Mr. Tisi joined us yesterday afternoon. And Mr. Golomb, too, I'm sorry.

Q. All right. Okay. Now, looking at the three reports that you have produced in the litigation involving Johnson's baby powder, I wanted to get an understanding of how those three reports relate to one another.

So you have the first report that you produced that was dated October 5, 2016. I believe that was originally produced in the Uhl case; is that correct?

A. I'm not sure the name of the first case, but it was in the -- some of the St. Louis cases, yes.

Q. All right. And when did you begin work on that report?

A. You'd have to look at my billing record, which I know was an exhibit to yesterday's deposition. I believe they started in 2015.

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Q. All right. And then you produced a supplemental report earlier this year, on August 29, 2018, and that's been marked as Deposition Exhibit Number 3, correct?

A. Yes.

Q. When did you begin work on the supplemental report that you produced at the end of August in 2018?

A. I want to say -- let's see. I want to say sometime in the summer. Maybe as early as May, but I believe May -- May, June time frame of 2018.

My billing would reflect that, so, again, we can pull my billing. And I would have called it preparation of the supplemental report in my billing.

Q. Okay. Why did you choose to draft a supplemental expert report?

A. So over the time I had worked on different trials here in St. Louis particularly, additional documents that were not cited in my original report became reliance materials based on their presentation at trial. So there were enough

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of those that I thought it was important to add to the original report with additional documents that I had reviewed over time.

Since October of 2016 through, let's say, the summer of 2018, there were a variety of additional documents that I had -- I had seen.

It was also my understanding that during that time period Johnson & Johnson had provided additional documents that weren't provided or available to me in 2016, so additional discovery that was now available to look at. So some of this is a matter of additional evidence that wasn't available when I wrote my initial -- my initial report.

Q. All right. Now when you say the additional documents became reliance materials in trial, what do you mean by that?

A. So additional documents that we refer to in trial that I use to support opinions that weren't necessarily specifically cited within the body of my report or described within the body of my report. They were likely on my larger

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reliance list, but they weren't things that were cited.

In other words, if you look at my original report in -- when I say the body, the paragraphs. I always put a reference list and then I'll have Bates numbers. So during trial, things that were from my larger reliance list that weren't specifically discussed in my report became support for different opinions that -- based on questions at trial.

Q. Okay. When you say these were documents that "we" refer to at trial, you're referring to yourself and attorneys representing the plaintiffs?

A. Yes, that's correct.

Q. Okay. And understanding that the purpose of today's deposition is focused specifically on the MDL, then you produced a report specific to the MDL on November 16, 2018, that we've marked as Exhibit 4, correct?

A. Yes.

Q. When did you begin work on the report that you produced specifically in the

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MDL?

A. Sometime right after -- I would say early fall of 2018, sometime after this -- the supplemental report was filed. Probably right after that.

Q. Okay. So is it fair to say that you began work on your MDL report after completing the supplemental expert report that has been marked as Exhibit 3?

A. Yes, that's correct.

Q. Okay. Who was involved in the drafting of the report that's been identified as Exhibit 4?

MR. MEADOWS: Objection. Hang on a second.

Are you asking about communications between attorneys and Dr. Plunkett?

QUESTIONS BY MS. BRANSCOME:

Q. Dr. Plunkett, none of the questions I will ask you here today are intended to elicit information that's protected by the attorney-client privilege.

So setting that aside, anything that you understand to be privileged, I can

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ask who the -- who was involved in the drafting of the report that was produced in the MDL?

MR. MEADOWS: Hold on just one second.

Ask the question one more time. I want to make sure we're not venturing into attorney work product realm here.

QUESTIONS BY MS. BRANSCOME:

Q. Dr. Plunkett, do you consider the report that you have issued in the MDL which is identified as Exhibit 4 to be attorney work product?

MR. MEADOWS: Objection. Don't answer that. That calls for a legal conclusion, and at this point I'm going to instruct you not to answer questions about how the report came into be.

MS. BRANSCOME: Are you instructing her to refuse to answer any questions that involve the development of her expert report?

MR. MEADOWS: I'm instructing

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her not to answer your last question.

QUESTIONS BY MS. BRANSCOME:

Q. Are you following your attorney's instructions, Dr. Plunkett?

A. Yes.

MS. BRANSCOME: At this point I would like to go off the record, please.

VIDEOGRAPHER: Okay. We are going off the record at 9:30 a.m.

(Off the record at 9:30 a.m.)

VIDEOGRAPHER: We are back on the record at 9:32 a.m.

QUESTIONS BY MS. BRANSCOME:

Q. Dr. Plunkett, other than attorneys, if attorneys were involved -- I am not asking questions about that -- were there any individuals who assisted you in preparing the report that has been marked as Exhibit 4?

A. There was no one that actually assisted in writing the report. I do -- when I did my literature searches, I had my husband help me retrieve articles that I identified for retrieval, but certainly there was no -- he doesn't participate in the

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actual review of articles or in drafting of the report. That's all my work.
Q. Okay. And when you say that your husband retrieved articles, was this simply -- what information did you provide him in order to enable him to retrieve a particular article?
A. So we use a service in Houston called Loansome Doc, which is affiliated with our local medical library system and also with the National Library of medicine and NIH libraries. So I give him an online search that I put into a clipboard. He takes that, makes the request or retrieves -- some of them will be free, and so he'll actually go to the websites for the -- and then put them into a folder for me.
So he does that physical part of it through the computer, but he doesn't -- he doesn't do the searches or decide which ones to retrieve. I do that.
Q. Okay. Did you have any discussions with your husband about the substantive content of the report that's identified as Exhibit 4?

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A. No.
Q. Does he do any evaluation -- for example, if you were to provide him a search and it generates multiple documents by a given author, does he identify additional articles that you might want to consider?
A. Only -- he has done that, but only with the streams of letters to the editor. So I ask him always if I'm pulling an article. Happens a lot at the New England Journal of Medicine or some of the other medical journals where there's pretty active letter to the editor correspondence that happens.
So I always say to him, "If there's any citation to this through the letter to the editor comments, would you please retrieve those," and so he will do that search to look for that.
Q. Okay.
A. And I'm not sure that that happened in any of these articles, but I'm talking my general process that we use.
Q. Okay. In terms of the relationship of the three reports that have

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been marked as Exhibits 2, 3 and 4 to each other, what is your -- what is your position with respect to opinions that you have stated or language you have used in Exhibits 2 and 3 that may not appear in Exhibit 4?
A. I don't think I understand what your -- what you mean by my position. Are you asking --
MS. PARFITT: And I'll object to that question.
THE WITNESS: Are you asking me to describe -- I mean, I could describe for you the overlap. I mean, there's not complete overlap. Is that what you're asking me or --
QUESTIONS BY MS. BRANSCOME:
Q. I am. Why don't you take a shot at it and then I may narrow my question, but I'm just trying to understand how the reports relate to one another.
MR. MEADOWS: Objection.
THE WITNESS: So they relate to each other, I would say, based on timing first, because obviously the first report was two years ago, and

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then many more documents. So that's how the 1 and 2 relate -- or Exhibit 2 and 3 relate to each other.
In the MDL litigation, I was asked to address very specific topics and things because there's a -- it's a different -- I don't know all of them, but there's a different set of experts that work in different litigations.
So my role in the MDL, I believe, is set out based on this report, whereas in the original reports I may have had -- I did have a broader role in some of those cases.
QUESTIONS BY MS. BRANSCOME:
Q. Okay. Can you describe for me your understanding of your role in the MDL?
A. It's my understanding that I have been asked to provide opinions related to the -- generally the toxicology of talcum powder products, including all the individual constituents that make up that product; to look historically back in time about what was known and when about the toxic effects of talc and different constituents within talc.

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And that was sort of the -- that's been -- I consider that sort of the meat of what I've been asked to do.

But separate from that, another part important part of my testimony or things I was asked to provide was an overview of the regulatory process for cosmetics and then the information that accumulated scientifically, how that related to what a company is required to do under the regulations in order to provide consumers with appropriate information about the safety of the product. So kind of the regulatory opinions, I guess you want to call it, that area.

I have sections on that, and I think you can see that by the different sections in my report where I set out different general topics.

And then I was also asked to address some of the issues related to how the information on the safety of talc has been disseminated publicly and also based on my review of different internal company documents, both from Johnson & Johnson -- or from Johnson & Johnson, Imerys, as well as

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the PCPC, which is the Personal Care Products Council, formerly known as the CTFA, to look at those interactions and how those companies set about to influence the process around the safety assessment of talc over the years. So different activities that happened with respect to the ISRTP meetings in the '90s, with respect to the NTP process at different points in time.

The CIR process, I think I cover, and I also talk a little bit about IARC, I believe, as well.

So the interactions of the industry with the science and then how that science ends up getting described within -- either to regulators or to bodies that are reviewing the science related to the products.

Q. You mentioned as one of the categories that you were asked to opine about in the MDL that you were looking to set about the influence that companies may have exerted over the regulatory process or PCPC.

When you began that analysis, did you start with the predicate belief that

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the companies had, in fact, influenced the regulators or PCPC?

MR. MEADOWS: Objection.

THE WITNESS: Not in my -- not when I first started this process. So that is -- those opinions actually go back into my original report. So that's not something, I don't believe, that was not covered in my original report or even in my supplemental report. I just have different -- some additional documents that I have reviewed.

QUESTIONS BY MS. BRANSCOME:

Q. Okay.

A. And this is something when I first evaluated the case and first started looking at the documents, those are opinions that I had formed based on my review.

Certainly by the time I drafted the MDL report, I think if you listened to my -- read my trial testimony, you understand I had those opinions at the time I started writing this report.

Q. Now, what I'd like to

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understand next is, are there -- of the topics that you just identified that you understand that you're offering opinions about in the MDL, which, if any, of those topics are in your view new as compared to the opinions that you have offered that are contained in Exhibits 2 and 3?

MS. PARFITT: Objection.

THE WITNESS: So I don't think any of the MDL opinions are new.

QUESTIONS BY MS. BRANSCOME:

Q. Okay.

A. I think that they may have -- they may -- they may cite to additional documents that haven't been cited to in the first two reports, but I believe there's a significant overlap even on the documents that are cited.

Q. And you mentioned that your role in the MDL is more narrow than the role you've served in other cases.

What topics have you opined about in other cases that you are not intending to opine about in the MDL?

A. So I am not doing general

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causation in the MDL, although I am indeed providing opinions on certain aspects of the cause and effect relationship such as -- you know, I talk about biologic plausibility, underlying knowledge about different toxicities of the compounds over time, but I'm not doing a full causation analysis in my MDL report, and hopefully you see that when you read the report.

Q. So as you sit here today, Dr. Plunkett, you are not intending to offer the opinion in the MDL that Johnson's baby powder causes ovarian cancer; is that correct?

A. Not in those words. I think if you read my report, I talk about the fact that Johnson -- it's my opinion that Johnson's baby powder increases the risk of cancer -- ovarian cancer, which is a different assessment than the way you stated it.

Q. All right. And it is -- as you sit here today, Dr. Plunkett, it is your understanding that you are not being offered to give a, as you termed it, a general

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causation opinion in the MDL, correct?

A. That's my understanding, yes.

Q. Now, you mentioned that the analysis as to whether a substance increases the risk of a particular outcome is different than a causation analysis.

Can you explain to me what you meant by that?

A. So I discussed this yesterday in my deposition. There's -- there's a process called risk assessment. Sometime -- in the area of consumer products you can also refer to it as safety assessment. And then there's the process of what I call general causation analysis, or full causation analysis.

So even though the types of information that are considered may overlap between those two, the outcome or the statements or the -- the way you go about assessing the information is a bit different.

Q. Explain to me how they're different.

A. So in a risk assessment, the process starts with setting out some basic

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principles of, first, is there a hazard, is the first step. Is there a hazard that would be relevant to human health.

Then looking at the data and determining whether that -- that body of data allows you to either quantify risk in some way or to qualitatively shows you that there's a change in risk based on exposure to the product.

So your statement may be as simple as there's an increased risk, or you can take data in a risk assessment and do a quantification such as in a -- a cancer risk assessment based on an animal data set. You might actually calculate a cancer potency factor, for example. Those kinds of things. That's another application of risk assessment. Same basic process but focusing just, for example, on one study.

My human health risk assessment or safety assessment, like the causation analysis, does look across all kinds of data, but my goal was not to analyze the data under the Hill considerations, which is what I would typically do, in order to go through

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the process of making that final opinion that indeed baby powder -- exposure to baby powder through genital application is a cause of ovarian cancer in women. That's -- to me, that's a different way to go about thinking about the question that you have to answer.

And also the -- some of the data that you evaluate is evaluated a bit differently. So, for example, in my increase -- in my issue of increased risk, I use the epidemiology as supporting evidence, but I'm really focused on -- on -- more on the underlying sort of the biologic information that we have that identifies hazard and risk. So looking at the animal data, the exposure potential for the product, and then using that along with what we know with the human experience to characterize risk.

Q. Is there a different level of certainty required to render a causation opinion than to render an opinion that there's an increased risk?

A. I don't know that I'd describe it quite that way but -- because to me it's a

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different process. I certainly have to be just as certain about what I say about risk when I do a risk assessment as I do about -- as I do when I'm doing a causation analysis.

I don't -- maybe you mean something else, so maybe you can -- I mean, I -- I certainly use the same basic standards in my mind, how I weigh evidence to do the different processes, but I go about them in a little bit different way when I do a risk assessment versus -- versus a causation analysis.

Q. In your view, does the strength of the evidence have to be greater in order to determine that an agent causes a disease, for example, than it does simply to say that an agent increases the risk of a particular outcome?

MR. MEADOWS: Objection.

THE WITNESS: I don't think I've ever thought about it that way. I would say to you that strength -- the strength of the association is a consideration under Hill that you apply the epidemiology data mainly, so

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that is a different consideration under causation than you do -- as you would do it in a risk assessment.

But the strength of the evidence, it's still a judgment based on your experience and training as far as whether or not there is enough information to be able to say that you believe that there is -- enough information to say that the risk is increased based on that exposure and those conditions and whatever the toxicity profile of that compound is.

QUESTIONS BY MS. BRANSCOME:

Q. Okay. We'll get into this more a little bit later, but when you say that a risk is increased, is there a threshold level of increase that you need to see in order to render an opinion in a court of law that an agent increases the risk of a particular outcome?

MR. MEADOWS: Objection.

THE WITNESS: So I need you to define what you mean by threshold. Are you asking me a specific

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statistical test you would apply, or what are you asking?

QUESTIONS BY MS. BRANSCOME:

Q. So understanding that for the most part if you're looking at statistical significance, you're looking whether the confidence interval crosses 1.

Are you following?

A. Yes, I know that, yeah.

Q. All right. And so when you're evaluating, though, whether a particular substance, in this case Johnson's baby powder, increases the risk of an outcome, again, in this case ovarian cancer, would it be sufficient for you if that increase was .01 percent, for example?

MR. MEADOWS: Objection.

THE WITNESS: That doesn't make sense to me, an increase of .01 percent, but maybe I can answer it this way for you based on what you've laid out there.

Certainly when I do a risk assessment and I make it -- if I'm going to make the conclusion that I

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believe that it's my opinion to a reasonable degree of scientific certainty that exposure to baby powder in women increases the risk of cancer, I'm having to rely on -- I do rely on data that allows me to draw conclusions because either there's a statistical significant finding found or the -- there's a consistency among the pattern of the data that shows there's information that fits together consistently. And maybe -- you want me to explain what I mean by that? No?

Whereas I think what you're asking is when an epidemiologist applies -- looks at a body of -- in a causation analysis looks at a body -- and I do this, too -- looks at a body of epidemiological studies and you weight the studies, obviously you're weighting the studies differently based on whether they have shown statistical significance or not, right?

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And it isn't that it's a one to one. If you have one positive and one negative, that isn't how you may decide to finally weight that evidence, but certainly you have to consider whether or not what was seen or reported is showing you something reliable -- or you can make a statement reliably about whether or not that finding was biologically significant. And biologically significant would typically be linked to a finding that has statistical significance in an epi study unless the study was not designed to be able to answer the question properly.

So -- and I've discussed that a little bit yesterday with Mr. Smith on the issue of power to detect. So that's something you do consider in epi.

But, yes, statistical significance certainly goes into your weight of the evidence there.

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QUESTIONS BY MS. BRANSCOME:

Q. Okay. You talked about you're intending to offer an opinion with respect to what a company is required to do under the regulations; is that correct?

A. Yes.

Q. Okay. What regulations are you specifically referring to?

A. So cosmetic regulations that exist within -- so it's the entire process as I describe how cosmetic -- what -- are cosmetics subject to regulation by FDA? Yes. What are the types of things that companies have to do before they're marketed, what does the company have to do once the product is on the market, those kinds of things.

Q. Have you ever worked directly for any regulatory agency?

A. No, I have not.

Q. And suffice it to say you have never been in a decision-making position within a regulatory agency, correct?

A. That's correct, I have not.

Q. Have you ever been in a decision-making position with respect to a company evaluating compliance with FDA regulations with respect to cosmetics?

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A. Yes.

Q. Okay. What is your experience with respect to that?

A. So that's -- one of the clients that I currently work for where I am asked to provide input on advertising, promotion and labeling of some of the products and then also some of the ingredients that are being promoted for use to -- to produce cosmetic products. So it's the idea of providing that advice over my understanding of the regulations what can be said and can't be said about certain ingredients.

This company is involved in making both ingredients but also some finished products now based on -- it's a large company that owns a lot of little subsidiaries.

Q. My question, though, Dr. Plunkett, was, have you ever been in a decision-making position for a company evaluating compliance with FDA regulations with respect to cosmetics?

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MS. PARFITT: Objection. Asked and answered.

THE WITNESS: So that's what I'm saying. They're relying on my input to make a decision on what will go in the materials.

QUESTIONS BY MS. BRANSCOME:

Q. Do you have decision-making authority within that company or, as you described it, are you providing advice and input?

A. I'm providing advice, but the things I'm advising on are the things that happened. So in other words, they don't have anybody in the company that understands the process of what they can say. So I -- I advise them that you need to remove this language or that this is more appropriate language. They make those changes, and then that is what is done.

So I agree, I'm not an employee of that company. I am a consultant working with the company, but it is a little different than some of the work that I do where I -- what I -- the advice that I'm

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giving is actually something that I know actually happened. Sometimes you give advice to companies, but it doesn't -- we have no idea whether the company actually follows our advice.

Q. My question is slightly different, Dr. Plunkett.

If you were to give advice to the company that you've referenced as having experience with cosmetic regulation compliance that that company chose not to follow, that company has the ability to ignore your advice, correct?

A. Yes, I would imagine that they could do that.

Q. Okay. Have you ever drafted regulations that relate to cosmetics?

A. Actually drafted a regulation? No, I have not.

Q. All right. You reference in your report language out of 21 CFR 740.1, and specifically -- you reference it in a few places. And I can direct you specifically to paragraph 22 in Exhibit 4.

A. Yes. I'm there.

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Q. All right. And do you see here you have replicated language from 21 CFR 740.1 that reads, "The label of a cosmetic product shall bear a warning statement whenever necessary or appropriate to prevent a health hazard that may be associated with the product"?

Do you see that?

A. Yes.

Q. And you added emphasis on particular portions of this sentence, correct?

A. Yes, I did that, exactly.

Q. All right. Now there's a clause in this sentence that states, "Whenever necessary or appropriate."

Do you see that?

A. Yes.

Q. You did not emphasize that language; is that correct?

A. That's correct, I did not.

Q. What is your understanding as -- what you describe as an FDA regulatory specialist of the meaning of "whenever necessary or appropriate" in 21 CFR 740.1?

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A. So it's -- first off, you would use the common English language definition. I don't believe that those -- I haven't seen a definition separate within the regulations. Sometimes there will be.

So based on that and my experience and the looking into what others have described about this, this is the idea of considering how the product is used, is one of the -- one of the concerns that you have, and whether or not the -- based on how the product is used and how the product is being sold, that in order to prevent a health hazard, a warning hazard -- a warning statement would be needed.

Q. Can you cite to me any language within the regulation or even supporting documentation, a comment, something of that nature, that would define "whenever necessary or appropriate" with respect to how the product is used?

MS. PARFITT: Objection.

THE WITNESS: I don't think I understand your question.

Are you asking me to cite to a

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reference or a part of the regulation where they explain it, or what are you asking me? Guidance document or --

QUESTIONS BY MS. BRANSCOME:

Q. Yes. Can you point me to anything other than your personal view of the interpretation of this language that would tie the requirement "whenever necessary or appropriate" to how a product is used?

MS. PARFITT: Objection. Form.

THE WITNESS: I'll have to go look for you whether there's a guidance that states it that way. This is based on my experience in dealing with the products in the past.

I think that's also consistent with what is described, I would say to you, within -- it's consistent -- what I'm describing to you, it's consistent as well with how the CIR standard for safety assessment is done, looking at the issue of the -- of the -- of the use.

QUESTIONS BY MS. BRANSCOME:

Q. When you say that you're basing

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your interpretation of the clause "whenever necessary or appropriate" on your personal experience, can you point me to something specific?

MS. PARFITT: Objection.

THE WITNESS: Are you asking me -- are you asking me if I've ever had a company that I worked for that that particular clause in here was extremely important to how we interpreted it? I don't think I can point you to that. I don't recall ever having to do that specifically.

Or is it something different you're asking me?

QUESTIONS BY MS. BRANSCOME:

Q. Dr. Plunkett, I asked you what your basis was for interpreting the language "whenever necessary or appropriate" means that it's related to how a product is being used, and the answer that you provided was that it was based off of your personal experience.

So I'm asking you, what is that personal experience that gives you the basis

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for that specific interpretation?

MR. MEADOWS: Objection.

MS. PARFITT: Objection.

THE WITNESS: So it's in my experience in dealing with companies that make products and what types of warnings are put or not put onto -- or not -- or on labeling. So I don't know how else to answer it other than that.

I can go back and look at the guidance documents to see if that is described in another way, but I don't recall that.

QUESTIONS BY MS. BRANSCOME:

Q. So as you sit here today, you're not able to provide me either with a third-party document or an independent document interpreting "whenever necessary or appropriate" as you've suggested today, nor can you give me specific example from your personal experience; is that correct?

MS. PARFITT: Objection.

THE WITNESS: Well, I certainly -- I'd have to go back and

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look at my documents in order -- the first part of your question, I'd have to go back and look. Off the top of my head, I can't tell what I would point you to.

On the second one, I think I was telling you, is I don't -- I've never -- I don't have a client that I've worked for where that part of the language was the only issue that I had to deal with when I'm looking at whether or not the product needs a warning or not.

So typically -- I'm just telling you that when I have looked at labeling for products and looked at the issue of does it need a warning statement, when I'm reading it as "whenever necessary or appropriate," I'm looking at whether or not the ingredient that I'm concerned about within the product, how that is used or what the exposure pattern would be, route of exposure, how those things might relate to how I would assess the

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safety issue at hand. And so that's what I'm trying to tell you.

QUESTIONS BY MS. BRANSCOME:

Q. Okay. You also have -- changing topics a little bit, in this -- in your report marked as Exhibit 4, if you could turn to paragraph 10.

On page 7, you state on the first paragraph on page 7, "In other instances I have directed others to perform searches on my behalf," and this is with respect to identifying documents for review in forming your opinions.

What did you mean by that?

A. So in addition to doing my own searches of the database, sometimes I -- I have called the attorney's office and asked them to -- to do a search for certain things that I'm looking for to add to. So in other words, I have a document I've identified. I'm looking for other documents like that in the large millions and millions of documents that are available. And so sometimes I will ask attorneys to do -- to look in the database for other documents like the ones

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that I've identified.
Q. And without getting into anything that would be -- that would call for information protected by the attorney/client privilege or attorney work product, what percentage of the overall searches for relevant documents from these particular databases that are discussed in paragraph 10 would you say that you have done yourself as opposed to directed others to do?
A. Well, initially when I first started searching, those were my own searches exclusively. I would say that more recently, in the last year, since I haven't added any real new areas but there's new documents that have become available, so anything -- any of the searches probably in the last year that dealt with new discovery that was produced, I would have asked the attorneys to do some of the searching in that for me. Like I'm looking for documents that are similar to this document that I cited in my original report around this same frame that may be discussing this same topic area.
So in the last year I have

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asked them to do that more than I have done it, but initially it was what I did initially.
Q. Okay. Do you keep any records of the various document searches either that you have performed or you have asked to be performed?
A. No, I don't. My record would be -- the initial -- the record would have been what I listed in my reliance list for you in the initial report, but since then it would just be what is going to be changing within my reliance list, looking at additional documents. That's the only way I could identify for you. That would be my -- my trail to know what was new and what was not.
Q. My question is slightly different. Understanding that you have provided to some extent a record of the documents, my question is: Do you have any type of record for the nature of the searches, what it was that you set out to identify in the database and how did you go about finding those documents?

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A. So that might cross over into work product because it's not my database, but I don't know how to answer that. I mean, I'm sure -- it's very possible that in the database you can track that, but I -- I don't know.
MR. MEADOWS: Okay.
THE WITNESS: I don't have anything saved on my computer that way, but when you go to the database itself, it's possible you could track that. I just don't have a record on my computer in my office.
QUESTIONS BY MS. BRANSCOME:
Q. When you made the decision at some point in time -- it may have been even prior to you issuing your first report -- that you wanted to look at company documents, did you set out specific categories of documents that you wanted to review?
A. Not so much categories but key words. So -- and areas. I guess areas is what I -- yes, I was focusing, for example, in my initial report on documents that described what was known -- what the company

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was discussing about cancer, ovarian cancer, cancer generally. So that was a key word used.
And then I also was linking that in different searches with different time periods such as the NTP review process and dates. You can, you know, narrow down by dates or by the CIR process. Those kinds of things.
So I did start with that, trying to understand what -- what is -- what was in the company files or in the files I had access to, the database, that dealt with those kinds of things because those aren't things that I could get to publicly. Obviously in the literature. So I had to -- if I wanted to understand what the company knew, I had to go into their database to find out, you know, what they knew -- what they knew or were discussing over time about the ovarian cancer issue or about asbestos in talc or about CIR process, things like that.
Q. Using the reports that you have produced, Exhibits 2, 3 and 4, really, and the full -- the entirety of the materials

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that you have produced in the MDL, is there any way that someone reviewing those documents, and those documents alone, could replicate the searches that you have conducted in the company databases?

MR. MEADOWS: Objection.

THE WITNESS: I don't know. That's a good question. I've never thought about whether you could replicate or not.

I mean, I think I've told you what I did. My strategy was to focus on topic areas. So I think you might -- by topic areas, if you use the same kinds of topics areas as described, I think you would come up with documents that -- what it focused down to.

For example, I also would sometimes, as linking those words, I might put in J&J documents only or Imerys documents only, because the database has a variety -- and the PCPC. There's some different ways by the Bates numbers that you can

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segregate documents as well. But I don't know other than that. That's all I can tell you.

QUESTIONS BY MS. BRANSCOME:

Q. You would agree with me that your report does not contain a complete explanation of the process by which you identify company documents to review, correct?

A. I haven't laid out my search structure, that is true.

Q. All right. Now, the articles that you have listed on your reliance list, have you read each and every one of those articles?

A. Unfortunately, yes, over time I have. Some of them I have only read parts of them. For example, if I started reading a document and I felt that it was something I pulled that really wasn't directly on point for an area I'm covering, I may not have read every word, but certainly I have been through each of those, yes.

Q. Are there any articles in your reliance list, that you maintained on your

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reliance list, that you read, but then once you started reading decided weren't relevant to the opinions that you were offering?

A. I would have to look to answer that for you. I don't know. If you want me to do that, I'd have to look.

Q. I ask you more as a process matter.

A. Oh.

Q. If you pull an article and you start reading it and you realize that it is not relevant to the opinions that you offered in this case, the example that you just gave, is it something that you would include in your reliance list?

A. Yes, I -- I have given you everything I retrieved. So if I retrieved it, you would have, yes, absolutely.

Q. Okay. So it's fair to say of the articles that are on your reliance list, you could not say as you sit here today that you have read each and every word of each and every one of them, correct?

A. That's correct. And I could probably tell you -- I could give you a

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little guidance in that possibly if I went to my list, I could try to pull some out that I recognize, but that's all I would be able to do for you.

Q. Okay. How did you go about identifying what articles you wanted to review in forming your opinions in the MDL?

A. So first off, I went back to what I already had. So my MDL report is a -- is a compilation of a lot of material that's in my first few reports. That was the basis for some of the things that went into it.

So I didn't -- I did do, though, a updating on literature searches for the MDL report, looking for anything new, for example, in the area, especially the area of cancer data or reports of dealing with ovarian cancer either -- or any articles dealing with the link between inflammation and cancer, ovarian cancer, generally. That's one of the areas I updated looking at.

And then I did -- I don't think I did any large, new searches, however, because honestly the areas covered here are a little narrower than what was covered here.

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I don't believe that there was any from the published -- the publicly available medical literature. There wasn't a need to do a whole new area of search. It was more updating the things that I've done in the past.

So it's a real easy search to update because you can just put in talc and cancer and just look at -- get lots, but you can then just start chronologically and look what was published in the last year, for example.

Q. Okay. Earlier when we were discussing the fact that you in some instances have asked your husband to pull articles, have you maintained any records of the searches that you have done with respect to scientific literature, including the searches that you have asked your husband to do?

A. I have not. It's possible that there are records on billing from the library that tells you how many I ordered at different times, but that is the only records, because we do have to pay the

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library for the retrieval.

Q. Okay. And if I understood what you said earlier correctly, you indicated that any article you have ever pulled for review, you have listed on your reliance list; is that correct?

A. Yes. And when I -- and let's just make sure we're talking about the same thing.

So, you know, in my reports I typically have articles cited in the report separate from the reliance list. So I'm talking about the reliance list, right? Okay.

So -- because I do -- I do usually -- I don't know whether I did that in this report, but I typically have a list of articles cited at the back called references, that is, things that you're actually seeing in the report body, and then there should be a separate reliance list sent to you as an appendix. I don't know what the appendix was.

Q. Well, so then let's clarify that. So, Dr. Plunkett, when you're

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referring to the reliance list, are you referring to the list of articles that begins on page 40 of Exhibit 4, or is there a separate document?

A. There's a separate document. So it -- that's -- I usually call reliance list the separate document. I call this references cited. So I apologize for that confusion.

So these, I have read every word. If it's in my reference list, those are not an issue of not having read every word, and these should all be cited somewhere in the report.

Q. Okay. If you could turn to paragraph 21 in your initial report.

A. Yes, I'm there.

Q. Okay. So we're looking at paragraph 21 in Exhibit 2. This is on page 10.

Do you see there is a sentence here that refers to -- it's referring generally to the topic of the ability of talc to migrate from the site of application to the ovaries.

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Do you see that?

A. Yes.

Q. And then the next sentence states, "This issue was discussed by scientific and regulatory bodies that review the toxicokinetics of talc."

Do you see that?

A. Yes.

Q. And in parentheses it identified EPA 1992, IARC 2010, and CIR 2013.

Do you see that?

A. Yes.

Q. Okay. And then if you could turn to Exhibit 4, which is your MDL report, at paragraph 43. It's on page 28.

Are you with me?

A. Yes, I am.

Q. You see that the exact same sentence appears -- well, not the exact same. It's been slightly modified to combine the first two sentences. But here you cite only to EPA 1992 and IARC 2010.

Why did you remove CIR 2013?

A. Because of my further evaluation since my initial report in 2016 of

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the process that was involved in the drafting of the CIR and the actual production of the report.

Q. Is it your position that the migration of talc was not evaluated as part of CIR 2013?

A. No. That's not my position, no.

Q. Okay. And so would the sentence that's contained in paragraph 43 in Exhibit 4, which is your MDL report, if you cited to CIR 2013 in the parenthetical there, would that not be an accurate citation?

A. I believe it would not be an accurate citation because I have formed opinions about the reliability of that document at this point in time.

So it has to do with -- I'm citing to authorities here that I believe are reliable as far as the discussion that I see, and it's a different -- I have a different opinion now about the CIR report, which I lay out in pretty detail, I think.

In fact, if you go to my section following this now in -- you'll

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understand one of the issues I had was the -- the difference in the evidence that was actually available once you dig into it a little further versus what they actually reviewed. That's one of the issues.

Q. And I'll follow up with some more questions about the CIR, but my question here is, the sentence in your report simply states, "The migration of talc internally after perineal application was discussed by scientific and regulatory bodies that review the toxicokinetics of talc."

Would it be inaccurate to say that as part of the CIR 2013 process that body did, in fact, discuss the migration of talc internally after perineal application?

A. It is true that they did discuss it. I just have an issue with the reliability of their findings.

Q. And so you made the decision to just remove it from the citation; is that correct?

A. Yes, at this point -- at this point, at this report, that's exactly right.

Q. All right. And then I had

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another question. In paragraph 43, you added two studies from your prior -- that were -- that did not appear in your prior report, and it was Gardner 1981 and Edelstam 1997. This related to animal studies showing that in some species talc can migrate from the lower to the upper genital tract?

A. Yes.

Q. Okay. Were those studies that you were aware of before drafting your prior reports?

A. I don't know that they -- I can't answer that without looking at my reliance materials for the original report. I did identify additional articles, and there's also additional articles cited here in earlier paragraph 43 that were not cited in my original report as well. I don't think I had the -- the Kunz article then cited. I'd have to go back and look.

So it's possible that they were in my -- when I say my reliance materials, my original report also had a larger list of literature I didn't cite. So I'd have to look. I can't tell you whether I had them or

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I did not.

Q. Okay. With respect to Edelstam 1997 study, do you happen to know the title of that article? Even an approximation would work.

A. It'll be -- should be back here. Just a second. If it's not here, that's a mistake.

Oh, here it is. "Retrograde migration of starch in the genital tract of rabbits."

Q. So you are citing that article for the proposition that animal studies have demonstrated that talc can migrate from the lower to upper genital tract?

A. Yes, I'm citing it because it's relevant to the issue of particle migration, which talc is a particle. So, yes, that's correct.

Q. Okay. But that study did not specifically deal with talc migration, correct?

A. No. Well, it -- it's relevant to talc migration, but you're exactly right, they looked at the starch migration, yes. Or

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particles that were starch, yes.
Q. We'll cover this in more detail, but is it your opinion that all particles have similar characteristics with respect to their ability to migrate in the genital tract?
A. It's my -- I don't know if I'd state it quite that way. What I would say is that the evidence shows that particles generally have the ability to move up the reproductive tract in women, yes, and that if a particle is one that is similar to talc or some of the other ones where the information has been collected, I would characterize that as being within that, quote/unquote, relevance of particles.
That doesn't mean all particles, but certainly in the ones that I have looked at and the data I've relied upon, there's a variety of different types of particles or substances that have been studied and shown to be able to migrate.
Q. So let's take Edelstam 1997 as an example.
Did you do any analysis that

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you can point me to that establishes that starch would have a similar migration pattern as talc?
A. So I would say that the paper itself shows -- talks about the movement of starch, but are you asking something different?
Are you asking me have I done a specific analysis of any differences that may occur between the migration pattern of starch and talc? Is that what you're asking me?
Q. That is what I'm asking you.
A. I certainly didn't do an in-depth analysis of the differences, no, but based upon my review of the literature, I believe that that paper is relevant to the overall question of migration of particulate through the reproductive tract, including particles of talc.
Q. Regardless of whether or not it was an in-depth analysis, can you point me to anything other than just your belief after having read these articles that starch and talc would have similar migratory characteristics in the human or animal

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genital tract?
MS. PARFITT: Objection.
THE WITNESS: Again, I haven't done an in-depth analysis. I mean, as a toxicologist, there are differences between starch and talc, absolutely. For example, starch would -- I would expect to be more easily solubilized within fluids, and so that could affect the ability of them to actually not migrate as well as a talc particle, which would be less soluble than the starch would be.
And there's -- I even -- there's a paper I have in here, and I can look for it if you want, that talks about that difference, and it's one of the issues of cornstarch versus talc, on whether or not you would expect to get the long-term chronic responses with the difference between those two substances.
So I do think there's difference, absolutely, as toxicologists generally. And the only

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reason I'm citing this paper is because I'm trying to be complete about people that have looked at this issue. And certainly it was a study that looked at this issue and talks about the movement.
But I wouldn't expect starch and the talc to have the same liabilities, and I also wouldn't expect them to move exactly the same speed maybe. That's very true.
QUESTIONS BY MS. BRANSCOME:
Q. So you would agree with me that Edelstam is not a study demonstrating that talc can migrate from the lower to upper genital tract, correct?
MS. PARFITT: Objection. Form.
THE WITNESS: I wouldn't say it that way. What I would say instead is that Edelstam is a study that forms the overall weight of the evidence for the ethics -- for the studies that are available that address the issue of migration, but certainly it is not studying talc. So I don't disagree

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with you there.
Unfortunately, the majority of the information that I have relied upon, and others such as the FDA in making their statements about migration, is not all directed studies just to talc. It's looking at the issue of particle movement.
QUESTIONS BY MS. BRANSCOME:
Q. Now, in terms of doing your risk assessment -- well, let me get back. We covered this earlier, and I want to return to it for a moment. Just to confirm: For your work in the MDL, you did not do a Bradford Hill analysis, correct?
A. I did not sit down and do a Bradford Hill analysis when I started writing this report. I have done a Bradford Hill analysis in the past, which is in my original reports, but I certainly did not redo a Bradford Hill when I sat down to draft my MDL report, that is true.
Q. Okay. Let me be more precise.
In the report that you have produced that contains a description of your

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opinions in the MDL, you have not set forth a Bradford Hill analysis in that document which is identified as Exhibit 4, correct?
A. That is true, yes.
MS. PARFITT: Objection.
QUESTIONS BY MS. BRANSCOME:
Q. And in fact, the paragraph that you -- or paragraphs that you have in your prior reports that reference a Bradford Hill analysis, those have not -- those have actually not been replicated in any form in Exhibit 4, correct?
A. Yes, because, again, it was not my role to do general cause.
Q. Okay. So then when we look at the methodology that you employed in reaching your opinions that are contained here in Exhibit 4, how would you characterize the methodology?
A. As I have in the report. I talk about it being a risk assessment or a safety assessment, that you could use those terms interchangeably here. And then I've also used a weight of the evidence as a tool to go through the different steps of the risk

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assessment.
Q. Okay. What publication would you direct me to that has used the same methodology that you have used to reach your opinions in Exhibit 4?
A. I think I cite you to -- cite you to some of those. You could -- well, the directly relevant one would be looking at the chapter on risk -- toxicology in the reference manual on scientific evidence.
You can also go to the NRC report where they -- it lays out the different steps that you use when you kind of break data apart into exposure versus response information.
And then I cite to -- there are some guidance documents that I cite to, and this is in paragraph 13. And I'd have to pull them out again to tell you which ones relate to different pieces because some of these are -- some of these documents are specific to only, for example, maybe one part of what I did.
But certainly the risk assessment process at IARC is -- they do what

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I call a hazard assessment. They identify hazard and they couldn't quantify risk, but the steps they go through are essentially the same types of steps that I went through as far as gathering data on not just response but also the potential for exposure and how that relates to the response.
And then also the data that I've collected on the biologic effects of talc, toxicology of talc, are also discussed within that document as well.
Q. Okay. Focusing specifically on the weight of the evidence tool, as you describe it, is there a particular document or publication that I would go to that could lay out the same process that you used for how you weighted certain pieces of evidence?
A. So the documents that I've cited for you in paragraph 13 talk about what weight of the evidence is generally, but if you read what it is, it's essentially a process that each scientist brings their experience, training and judgment to.
So I try to lay out for you in my discussion of the literature my thought

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process as I review each piece of information, and that is what you do as part of weight of the evidence. You gather all of the relevant information that you can find that address the question you're trying to answer, and since I'm looking at both exposure and response, I gather different pools of information.

Q. You would agree that there are ways to do a weight of the evidence assessment of published literature that assign, for example, quantitative values to particular pieces of evidence, correct?

A. Certain individuals have put together, but there's no one general accepted process that everyone uses. So I -- that's the issue. Again, there are certain -- certain cases where I've seen that done, and then there are many -- most cases that it's not what's done.

Q. Okay.

A. Another body, by the way, that I -- it's new. It's not in paragraph 13. I just want to make sure I tell you that so we're clear. If you look at the Canadian

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document, they also -- in fact, a lot of what they have, you'll see the same literature described within my assessment as well.

Q. So using the Canadian assessment as an example, for instance, in that assessment there were actually values assigned to particular pieces of literature, correct?

A. Mainly the epidemiological literature, that is true. Again, but I'm not doing causation, so I didn't approach it that way.

But certainly if you look at what I did, it's consistent with that because I talk about the differences between the limitations of a case-control versus a prospective study. I talk about both the positives and the negatives within the database, but I don't lay it out in a table like they do. But it's certainly the same basic process.

I was actually quite surprised at how similar the database of information that they reviewed was to what I honed in on as well.

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Q. Okay. As you were forming your opinions, Dr. Plunkett, about whether or not there is a risk associated with the use of Johnson's baby powder with respect to ovarian cancer, how do you keep track of the pieces of scientific evidence that you have reviewed and the respective weight that you give to them?

Presumably you did not read everything in one day, for example?

A. No. That's correct. So I typically will -- I typically will save the papers -- when I read the papers, I will often highlight in yellow information that I think is going to -- will be extremely relevant. I don't put notes on the document. I highlight in yellow on the PDF file to use that to write.

And I also start drafting report very early, which then gets overwritten and actually ends up looking like an outline that eventually becomes the report.

So one of the ways I keep track of things is I may put a paragraph name that

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I know I'm going to write, such as exposure migration, and then I -- as I'm reading a paper, I'll type in a paper -- the ones that I believe are important to my overall assessment. So I will do that as I'm -- as I'm going through the evidence.

So that's one of the tools I use, but I don't keep notes. I just kind of use that as a living document that eventually becomes a report.

Q. Do your opinions ever change as you read additional pieces of scientific evidence?

A. Yes, it does. It may change. And it often -- often the changes, though, are not that I believe -- with the exception of epidemiology. In other areas. Epidemiology is a little bit different issue when you're reviewing studies.

But on toxicology I always start with reviews and regulatory authorities, looking at what others have said generally about the toxicology. And so even though I may refine opinions differently or I might change, I certainly wouldn't agree to

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work on a project to start with if my initial reviews on hazard, for example, didn't convince me that I believe that there is a hazard. But you refine it from there. That's exactly right.

So there are cases, however, where I'm asked to work on a project where there is no review or regulatory authority or any kind of assessment over a period of years, and in those cases there are times when I start working on a project and I stop and say, "I can't do this." Because that happens, yes.

So opinions do change sometimes based on review of additional information.

Q. Is there any documentation that you've produced either in your report or otherwise in the MDL that would allow someone reviewing the material to understand the order in which you reviewed materials or the specific weight that you assign them?

A. So order of review, no. I don't think you would know that other than -- you will note order of review if you look at the differences in the literature cited in my

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original report versus in the MDL.

So in my original reliance list, if there were documents that weren't there and they're now here, obviously that tells you it was a review.

On the issue of a -- of the weight of the evidence process, the only answer I can give you for that is that articles that I believe are -- are reliable, are relevant and are -- those are kind of the -- you look at the reliability of the studies, whether they're peer-reviewed or not or if they have proper controls put into place, things like that, whether or not the -- they're relevant to the question at hand. That you can get from looking at how I discuss them in the document. But certainly there's no, like, summary of that.

But certainly -- I think you understand -- you should understand when you read my report what weight I'm giving based on how I'm describing those -- those materials. I mean, it's --

Q. Well, for example, you do have different studies that you've identified in

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your report that have been criticized by others at some point in time, correct?

A. Yes, that's true.

Q. Okay. Now, in some instances you state that you then give little weight to those studies, correct?

A. Yes.

Q. But in other instances you find the criticized study to be helpful and informative, correct?

A. That's true. Because, again, judgment -- as anybody does weight of the evidence, different scientists can have different judgment.

Mainly, I think, when I look at the differences in that -- in that regard, I think you should pay attention to what the person is. So as a toxicologist, I may view a certain type of -- piece of data very differently than an epidemiologist may view it, as far as the reliability or the relevance, because we're coming at it from a different training and experience and judgment -- set of judgment on what is important to a toxicologist when I'm talking

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about risk versus how an epidemiologist might talk about risk.

Q. Could two different toxicologists review the same piece of literature and give it very different weight?

A. I don't know about different weight, but they certainly -- I know people come to different conclusions based on their overall assessments. That happens, definitely. I mean, there are always going to be individuals that look at things differently.

I know in this case there are people -- I've seen defense experts that reports in -- not in the MDL but in other cases, where people disagree with some of my opinions, and I disagree with their opinions. That happens.

Q. Okay. And so if I were -- well, let me just ask something. You have not provided any sort of quantitative assessment of the weight that you gave different pieces of evidence that you cite in forming your opinions in the MDL, correct?

MS. PARFITT: Objection.

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Misstates her testimony.
MR. MEADOWS: Objection.
THE WITNESS: So I don't report for you a table where I quantify that, that is correct, but certainly that is -- because, again, based upon looking at the way that I was trained and the documents that I'm talking -- I'm pointing you to to describe how to do weight of the evidence, it is not -- it is not a numerical exercise, how many here, how many there, this one gets 5 points because of this or 6 points because of this.
It's more an issue, again, of judgment. It's the idea of looking across all of the available information and determining whether or not, based on that, it's your opinion that there -- that, for example, talc -- talc's toxicity profile includes cancer. That's one of the judgments -- weight of the evidence judgments you make, for example.

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QUESTIONS BY MS. BRANSCOME:
Q. So -- but, Dr. Plunkett, just to be clear, you do not provide a numerical value to the particular pieces of evidence that you have considered as part of your weight of the evidence assessment in the MDL, correct?
MS. PARFITT: Objection. Form.
THE WITNESS: So I do not provide a numerical value as you see it laid out, for example, in the Canadian table, but certainly I do judge articles that I include in my weight of the evidence based on a system that includes different considerations such as -- like I said, peer-reviewed or not, that makes an issue.
Whether or not the study that's being reported is the only one -- the first or is this something that is -- that is describing an assessment that's been done by someone else and so you see a repetition or a consistency among the studies that

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you're looking at.
The robustness of the data. For example, the NTP GLP quality animal study, very high quality in the weight of the evidence. And I talked to you about that. In fact, it -- even though people criticize that study, that study is very valuable for looking at biologic changes that are consistent with a carcinogenic mechanism being initiated.
So even though you may say that you can't quantify risk from that animal study as far as calculating a cancer potency factor, what you can do is use that study of high quality to make judgments within a weight of the evidence for risk.
QUESTIONS BY MS. BRANSCOME:
Q. Dr. Plunkett, you understand I have seven hours today, and I -- while I'm very interested in the answers that you give, if we could just -- we will get to things like NTP when we get there, if you could just attempt to answer the question that I've

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asked.
I simply asked the question: Are there numerical values assigned to the particular pieces of evidence that you have considered as part of your weight of the evidence assessment in reaching your opinions in the MDL; yes or no?
A. And I said to you, not in the way that it's done -- I assume you're referring to something like what was done -- what's in the Canadian epidemiology table. I have not done that, no.
Q. Okay.
A. That's exactly right.
Q. Have you provided a qualitative chart, for example, of the evidence that you have considered in forming your opinions in the MDL?
MS. PARFITT: Objection. Form.
THE WITNESS: I don't know what you mean by qualitative chart. I certainly have -- I certainly, I believe, have given you qualitative descriptions of my weight within my discussions of each study, yes, I have

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done that.
QUESTIONS BY MS. BRANSCOME:
Q. You mention in response to the prior question that you have a system for weighting the pieces of evidence that you have reviewed.
Can you point me to paragraphs in your report marked Exhibit 4 that would outline in detail the system that you used to apply different weight analysis to different pieces of evidence?
MS. PARFITT: Objection. Form.
THE WITNESS: And I think I answered that, that there's no system written down by anyone. But what there is, instead, is if you read these -- if you read these descriptions of use of weight of the evidence that I've cited in paragraph 13 as well as the discussion of methodology in the Canadian document, that is consistent with what I do. It's the idea that you start with a literature search for peer-reviewed, publicly available

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information. You look at the quality of the studies, the statistically significant findings. Those are all things that are discussed within these documents I'm pointing you to.
QUESTIONS BY MS. BRANSCOME:
Q. Now, you --
A. But it's -- it's -- I don't know of anyone who has written down a specific system that applies in all circumstances, no.
Q. Okay. Have you written down a system that applies specifically in this case?
A. I think I have tried to do that for you when I describe what I did.
Q. Okay. You just referenced the fact that your system can be found in the Canadian document.
You agree that the Canadian analysis was actually published or produced after you had completed your report in the MDL, correct?
MS. PARFITT: Objection. Form.
THE WITNESS: Certainly it was

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published afterwards, and what I thought I said to you was that if you look at that document -- it's not in paragraph 13, but if you look at that document, it lays out a process. And I wouldn't call it a system. It's a process. It's a process by which you screen information for relevance to the question being asked and how, then, based on that, you look at characteristics of that information such as -- and I tried to give you some of those.
And I've said this before in depositions in these cases. You know, you look at the issue of whether or not the study was peer-reviewed, whether or not there was statistically -- statistical significance or at least statistics applied to the data. What was the quality of the study as far as the size in order to be able to answer the question being asked. Those are the kinds of things that you look at.

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And then also the question -- when you're looking at a specific question, you may pull in -- like you asked me about the starch particle. You may pull in things that you give less weight because obviously that's not just talc, that's starch, and you have to consider that. So that is part of the process.
QUESTIONS BY MS. BRANSCOME:
Q. Dr. Plunkett, the question I asked you simply was: The paper that you reference that contains some detail about the Canadian analysis, that was published after you completed your report that's marked here as Exhibit 4; is that correct?
MR. MEADOWS: Objection.
THE WITNESS: Yes, and I believe I answered that at the start. I usually try to answer your question, and then I try to explain further some details I think are important context on my answer.
QUESTIONS BY MS. BRANSCOME:
Q. I understand that,

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Dr. Plunkett. You have given many depositions. You understand I can ask you for more detail if that would be helpful to me.

If you could, just focus on the question that I asked, and we can explore additional areas if that's something I'm interested in doing.

Okay?

MR. MEADOWS: Objection.

She's --

MS. BOCKUS: Break?

MR. MEADOWS: After I finish my objection.

She's going to answer the question as thoroughly as she feels like she needs to answer the question based on the way you ask it.

Want to take a break now?

MS. BRANSCOME: We can go off the record.

VIDEOGRAPHER: We're going off the record at 10:41 a.m.

(Off the record at 10:41 a.m.)

VIDEOGRAPHER: We are back on

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the record at 10:56 a.m.

QUESTIONS BY MS. BRANSCOME:

Q. All right. Dr. Plunkett, we started talking a little bit about the CIR analysis that was done in 2013.

Am I correct you no longer consider that reliable? Is that your opinion?

A. Yes.

Q. Okay. And you identify in your report marked as Exhibit 4, I believe it's paragraph 56?

A. Yes, that's correct. And I think I talked about it later on as well, but definitely I do here.

Q. Okay. And in paragraph 56, you state that the CIR panel failed to account for all the studies that informed on the issue of migration of particles such as talc upwards through the reproductive tract.

Is that your opinion?

A. Yes.

Q. Okay. And then you state that because of that you assign, quote, little weight to the conclusions reached by the CIR

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panel; is that correct?

A. Yes.

Q. And so is it your view that a study or an analysis that reaches a particular conclusion should be assigned little weight if it fails to consider all relevant scientific evidence to the issue that it's evaluating?

MS. PARFITT: Objection.

THE WITNESS: I think it depends on the situation, but that could be the case, yes. It depends on -- on the -- depends on -- I think it would depend on each case, the question being asked, and what was omitted. But, yes, I think it could.

QUESTIONS BY MS. BRANSCOME:

Q. Okay. And in this situation you identify -- I believe you claimed that eight human studies were not considered by the CIR 2013 panel; is that correct?

A. Let me look at the number, but that sounds about right. Yes.

Q. All right. And returning, actually, to your prior answer, you said that

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the failure to consider all relevant scientific evidence on a topic would lead you to assign little weight to a particular conclusion. You said that that could happen.

Under what circumstances would you assign a conclusion little weight for failing to consider what you consider to be all relevant pieces of scientific literature?

A. Well, I think it depends -- well, the reason I specifically addressed that in this case is because that was -- the conclusions about migration is the main reason why the CIR panel then draws additional conclusions later on.

So my issue is, migration was key to what -- the decisions they made about the safety issues of talc. And so in that particular case, this -- this failure to consider all the evidence was extremely important, in my view, and I gave it little weight.

There might be a situation where some -- for example, you may only look at six or eight studies, even though there may be dozens out there. You may have a

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reason for why you only looked at six or eight, or it may be -- and as a result you may lay that out and, therefore, you may still give weight to conclusions drawn. Or it may be that the six or eight are -- studies that you discuss are not -- the weight is not affected by what you've omitted.

I believe that the weight is affected by what is omitted when you look at some of the articles being review articles, which give you an understanding of what was generally accepted within the scientific community when you get to reviews, those kinds of things. So it really is a case-by-case basis.

But certainly I do believe that it is possible that in another circumstance where things are omitted you would come to the same conclusion, that you give those conclusions less weight.

Q. Is there a way, if someone were try to replicate the weighting of particular evidence based upon your process, for them to know whether or not the omission of a

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citation of certain studies means that a study should be given little weight or whether it wouldn't affect the weighting of that scientific article?

MS. PARFITT: Objection. Form.

THE WITNESS: So I think this is the issue of judgment, training and experiencing that is applied to all such assessments, and this is why different scientists may come to different conclusions. But certainly it is -- it was important to my assessment on this issue because of the prominent role that the CIR report gives to their conclusions here for why they then drew conclusions about safety. And so that link was extremely important.

MS. BRANSCOME: Can we pause for just a moment?

VIDEOGRAPHER: We are going off the record at 11:00 a.m.

(Off the record at 11:00 a.m.)

VIDEOGRAPHER: We are back on the record at 11:01 a.m.

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QUESTIONS BY MS. BRANSCOME:

Q. Okay. Of the eight studies that you identify on page 37 of your report that you contend the CIR panel did not account for, do any of those eight studies specifically discuss the migration of talc in human subjects?

A. No, I don't believe they do, but there are a couple of these studies that I found to be extremely important if you want me to explain that to you.

Q. Do you break out in your report in any other paragraphs which of these eight articles you consider to be extremely important?

And if you could just point me to paragraph numbers, that's good enough if you have, in fact, broken them out.

A. I have. I -- this whole section I break -- I talk about each one individually. So I think you can tell by what I read -- what I'm discussing what I thought was important and informative about each of those.

Q. Do you rank the eight studies

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in any way by their importance to you?

A. Not with any numerical rank, no, but certainly I think I do that for you when I talk about the studies. I give you an understanding of ones that I think are particularly informative and ones that are not.

So, for example, I weight the human data -- I think I tell you that -- more than the animal data because of the differences between the reproductive tracts of humans versus animals generally, upright versus -- upright and habits and things that humans do that relate to insertions in and out of the reproductive tract, I guess is a nice way to describe it, versus an animal, that those can have, and then also the differences between animals and humans in terms of bursal sac around the ovary, those kinds of things.

So I do -- that -- I guess that ranking I do give you here. I tell you that I think these -- I think that the most relevant are going to be the human studies versus the animal studies.

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Q. Right.
So my question specifically is, where would you point me to in your report to understand the weight that you gave each of these particular eight studies?
A. At my descriptions of those studies and what I describe. That's all I can tell you.
Q. And I'm just asking, Dr. Plunkett, can you point me in the report to where that discussion takes place?
A. It takes place -- I have a discussion for each study, and I would -- and if you read what I say about each study, I try to go through what the strengths and weaknesses of those studies are.
And so those -- that would be, let's see -- you want me to give you the starting paragraph?
Q. So, for example, Parmley and Woodruff. Can you point me to where in your report you discuss Parmley and Woodruff, such that I can understand the weight that you gave that particular study?
A. So the year of it is...

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So I think I discuss it in paragraph 44, and so I describe for you what important information is in there, which is the information that I take as forming part of my weight of the evidence.
So one of the most important things is what -- they have a figure they show, and they're showing -- which is one of the unique figures in all of the published literature. But it talks about the differences between the female reproductive tract and the male reproductive tract, and it shows the actual -- it talks about a discussion of movement from substance in the environment through -- into the vagina, into the fallopian tubes. So it's a paper that addresses that very specific issue.
Q. So my question to you, though, is, where do you have a discussion of the weight that you give to these particular articles?
A. So the discussion of the weight has to do with the information described. I don't give them a numerical ranking. I told you that.

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So what I do is, when I'm discussing about these -- all of these papers here contribute to my weight of the evidence. And if it's a human study, I'm giving those more weight than I'm giving animal studies. And that's described.
And then within papers I'm pulling out information that contributes to what I think is important about what the study says, and that -- and the importance of what is described within the study contributes to my weight.
And I don't know how else to describe it to you. That is the process that scientists go through when they evaluate data.
Q. And so my question to you: Earlier you said of these eight studies, some of them were particularly important to you.
How would I, using only what's written in your report, understand which of those eight studies was of particular importance to you?
A. So it would have to do with what I discuss about the study. So I'm

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telling you, when I -- if you look through this entire section, this is the Parmley and Woodruff paper. It is important because it addresses the specific issue of movement of environmental substances from the outside to the inside. So I'm giving that importance in my evaluation because of what that author is actually discussing.
I don't know how else to describe that. I apologize. I mean, to me, weight of the evidence is a process that scientists use bringing their training and experience and judgment, and it's not a numerical process across the board, it just is not, based on the way weight of the evidence is used within science.
Q. Now, Dr. Plunkett, though, you would acknowledge that if you wanted to assign numerical values to the studies, that has been something that has been done by other authors and other authors on whom you rely, correct?
MS. PARFITT: Objection. Form.
THE WITNESS: I don't believe that's true. I'll need to look -- I

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don't believe that's true with respect to the biological information. I believe it may be true with respect to the epidemiology studies.

You want me to look real quick to confirm that? I can do that really quick, but...

QUESTIONS BY MS. BRANSCOME:

Q. I'm simply saying, could you assign a numerical value if you chose to do so?

MR. MEADOWS: Objection. Objection. Form.

THE WITNESS: And I'm -- what I'm trying to say to you is I think that I -- that there is no one set of rules that you would assign in order to do that for all the types of studies that you weigh.

I would agree that I have seen it routinely done -- well, not routinely, but I've seen it done within the epidemiological community when they go through the epi data. But not -- it's not something that

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I've seen done when you talk about weight of the evidence as part of a human health risk assessment. That is not something that scientists typically do as far as giving numerical rankings.

QUESTIONS BY MS. BRANSCOME:

Q. You're familiar with the National Cancer Institute, correct?

A. Yes, I am.

Q. All right. They are considered to be the nation's leader in cancer research, correct?

MS. PARFITT: Objection to form.

THE WITNESS: The National Cancer Institute?

Yes, they are. I don't know if they're "the" leading, but they're one of the leading, that's true.

QUESTIONS BY MS. BRANSCOME:

Q. Okay. And you're familiar with publications that they issue called physician data queries?

A. Yes, I am.

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Q. All right. And you are aware that there is, in fact -- called PDQs, correct?

A. That's the abbreviation, yes.

Q. Right. And you're aware that the National Cancer Institute has in fact published a PDQ that addresses a potential connection between talc and ovarian cancer, correct?

A. I'm aware of several that have been done over the years, but, yes, I'm aware of that.

Q. And have you reviewed those?

A. Yes, I have.

Q. Are they listed on your reliance list?

A. No, but they're listed within the materials as discussed within my depositions, and I thought -- and my testimony. I thought that was part of my reliance list. I believe that it -- it was in my reliance list, is encompassing all of the testimony as well as the actual documents. Maybe I'm mistaken, but that was my understanding.

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Q. Okay. If they are not on your reliance list, should they be?

A. I believe that they are on my reliance list by it having been pointed to as part of the testimony that I have given and the documents that I have relied upon during testimony.

Q. Okay. And you are aware that they have issued a PDQ that -- on the website as of today, correct?

A. I haven't looked today, so I'm sure -- but I know that -- I don't believe it has been removed, so I believe that there is something there, yes.

Q. All right. And what is your understanding of the position stated in the PDQ with respect to a possible link between talc and ovarian cancer?

A. So I'd have to look at the one today to tell you what it says, but it's evolved over time and it's changed over time, and I have specific opinions that I've expressed at trial about that issue.

Do you want me to go into that details or I mean --

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Q. I'm not asking about your opinions about what their position is. I'm simply asking you, Dr. Plunkett, the most recent NCI PDQ that you have reviewed, what is the position that the National Cancer Institute has taken with respect to the relationship between talc and ovarian cancer?

A. So I would want to pull it out to give you the specific statement of their position, but their position has changed such that later in time they've weakened the link -- their statements about the link between ovarian cancer and genital talc use.

So it used to be seen as a cause, and now I believe it's not seen as a cause. I don't know the exact language, though. I'd have to look at it as -- maybe risk factor is the better word to use.

And I need to look at the most recent one. And that would be the best way. Let's just see what it says.

Q. Okay. 'Cause is it your position as you sit here today that the National Cancer Institute has ever issued a statement that talc causes ovarian cancer?

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A. I believe it was listed as a risk factor for ovarian cancer in the older PDQs.

(Plunkett Exhibit 7 marked for identification.)

QUESTIONS BY MS. BRANSCOME:

Q. I do have a copy here. Just for the sake of the record, we will mark this as Plunkett Deposition Exhibit Number 7.

Handing a copy to you, Dr. Plunkett, do you recognize the document that I just handed you that's marked as Exhibit 7?

MR. LOCKE: What's the date of that?

MS. BRANSCOME: This was printed on December 14, 2018.

THE WITNESS: It's -- the updated date is June 22, 2018, if that helps.

MR. LOCKE: Yes, thank you.

THE WITNESS: I have seen this one, yes.

QUESTIONS BY MS. BRANSCOME:

Q. All right. And you can review

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any -- whatever portion of this is helpful to you.

And then if you could answer my question, Dr. Plunkett, of what is the position as stated in Deposition Exhibit Number 7 of the National Cancer Institute with respect to the relationship between talc and ovarian cancer?

A. So I would be looking at the section on page 12 of 18, and maybe you're looking somewhere else, but that's where they actually talk about perineal talc exposure. And it's under the section where they have now moved into factors with an adequate evidence of an association and they describe it here. So they're calling it an association where the weight of the evidence is not adequate to support that association.

Q. All right. And so the first sentence of the section under perineal talc exposure states, "The weight of the evidence does not support an association between perineal talc exposure and an increased risk of ovarian cancer."

Did I read that correctly?

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A. You did read that correctly.

Q. All right. And it indicates that "results from case-control and cohort studies are inconsistent."

Did I read that correctly, Dr. Plunkett?

A. You did.

Q. And the question that I would ask simply is, do you discuss the National Cancer Institute PDQ in the report that you've issued in the MDL, which is identified as Exhibit 4?

A. I don't specifically discuss this document, no, I do not.

Q. Okay. And you understand that the NCI PDQ did a weight of the evidence analysis that followed a formal evidence ranking system, correct?

MS. PARFITT: Objection.

THE WITNESS: So I -- it's not laid out here, but they do have a process they use.

Is that what you're asking me?

QUESTIONS BY MS. BRANSCOME:

Q. Yes.

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A. Yes. And again, they're ranking the epidemiological data, and so I understand that that is there, yes.
Q. Now, you've said a few times that you could qualitative -- you could give a quantitative weight to an epidemiological study, somehow suggesting that it is different from other types of studies.
What is it about a toxicological study, for example, that would prevent someone from giving a quantitative weight in a weight of the evidence analysis?
A. Because it is just what is typically done and not done. There are certain practices within the community, what is kind of -- I would say that scientists use routinely, or scientists have used. Not all scientists give numerical rankings to epidemiological data either, because even within a Bradford Hill assessment, when you use the considerations, there's no requirement for ranking studies in order to meet the requirements of use of that methodology.
Q. Okay.

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A. But I have seen it done in the epidemiology community, and that is the most common place I see it. I do not see other toxicologists that are assessing animal studies and in vitro studies doing it that same way.
When you do a human health risk assessment, that isn't routine practice to do numerical rankings on studies.
Q. Okay.
A. At least in my experience and in my training, and I was trained in the use of risk assessment by one of the individuals who actually invented the process.
Q. Okay. Okay. But do you consider the epidemiological evidence as part of your risk assessment in the MDL?
A. I do, because I'm looking at it in the context of what is out there and what's available. I don't always have human data when I do risk assessments, but in this one I do. So I do consider them, yes.
Q. Okay. Did anything prevent you from doing a quantitative assessment of the weight that you were giving different pieces

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of epidemiological evidence?
A. If by -- you mean prevent, was someone stopping me from doing that, no. But if you ask what would be standard practice based on my experience, I would not be doing that.
Q. Has anyone -- and I'm not referring in this case to any attorneys. But has anyone reviewed your -- the weighting that you gave specific pieces of evidence as essentially a form of a peer review process?
A. If by that you mean have I submitted my opinions for publication, no, I have not done that. Part of -- that's partly driven by my understanding of the evidence that I reviewed, that some of it may not be something that I should be discussing necessarily in a public form outside of the cases I'm working in.
But certainly I have not submitted it for publication, if that's what you mean. No, I have not done that.
Q. Okay. Has the methodology that you have used in the MDL, has that been -- have you submitted any type of analysis using

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that methodology for publication even outside of particularly looking at Johnson's baby powder, for example?
A. Yes, in -- if you look at my publications that describe risk assessments that I have done. So the one that would come to -- to play that's similar as far as the scope of the weight of the evidence would -- at least with the animal and the in vitro studies, would be the paper that I published on copper, looking at the database of copper and identifying points of departure and target organs and risk -- risk issues based on copper use in humans, trying to set a -- understand what a safe exposure level could be to copper in water. And that was published -- that actually was one of the papers that's published with Dr. Krewski, who is one of the authors of this risk assessment in Canada.
Q. And is it your position that you follow the same methodology in what you've reported in the MDL with respect to Johnson's baby powder that you did in your analysis of copper?

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A. Yes, with the process of going through all of the publicly available information, putting it together based on its relevancy and reliability.

We did a process where we grouped it based on animal versus human, just like I've done here. And we call it the bins, but it's the same idea. I have a bin of human idea, I have a bin of animal data and a bin of in vitro data. And so, yes, the process was very, very similar.

Q. Okay. Returning back to some documents that you chose not to cite in your report, you do not discuss the Gonzales 2016 study in your report for the MDL, correct?

MS. PARFITT: Objection. Form.

THE WITNESS: I'll have to look. It is not cited in the reference list to my report, that is true. So that means it would not be mentioned specifically in the body of the report.

QUESTIONS BY MS. BRANSCOME:

Q. You're familiar with the Gonzalez 2016 study, correct?

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A. If you want me to talk about it, you'd have to pull it out for me, but I know the name, yes.

Q. Okay. And it was looking at an association between the perineal use of talc and ovarian cancer, correct?

A. That, I'd have to look at it to tell you. I believe it was a human study that would be consistent with that, but I need to pull it out to look at it.

Q. All right. Do you, as you sit here today, do you know why you did not discuss it in your report?

A. I wasn't doing a full causation analysis in this report, so as a result I'm not trying to characterize every piece of human data. But I certainly am looking at the consistency across the studies, and that's what I've done.

And I mention it here. I do think I mention here that there are studies that came to different conclusions than the ones that I'm specifically describing.

Q. Okay. And so why is it that -- why is it acceptable for you to choose not to

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include something like the Gonzales 2016 study, but yet you will disagree the 2013 -- the CIR 2013, you will give it little weight for not discussing particular studies?

A. So that's a very different exercise. You want me to explain my thinking on that? I can do that for you, but I believe that's apples and oranges question.

My reasons for giving little weight to the CIR overall assessment versus my weight or the assessment I make of an individual piece of data, that's different. And that's what you're describing for me.

And I believe Gonzales is in my overall reliance list, so I have read Gonzales. It is something that I have considered; it's not something that I've cited in my paragraphs. So it doesn't mean it didn't go into my weight of the evidence, because I do have it and I have reviewed it. I just don't recall the details on it.

Q. Is it your position as you sit here today that you know for sure that the CIR panel did not -- was not aware of or even considered any of the eight studies that you

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contend the omission of which makes it of little weight?

MS. PARFITT: Objection. Form.

THE WITNESS: I would say I'm 99.9 percent sure, based on the process that is -- that goes in. And if you want me to explain, I'll tell you why I feel that level of surety.

You know, I can always say that maybe there was someone that came to the panel that did a search on their own, but that is not what's done. The individuals that come to the panel are given a body of information provided to them in written form that they review. So it's not like they -- they have access to anything that isn't cited in the actual report.

QUESTIONS BY MS. BRANSCOME:

Q. Okay. The eight articles that you discuss that are not mentioned in the CIR panel's work, they are publicly available pieces of scientific literature, correct?

A. Yes, which was why it's interesting to me that those were not grabbed

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and included within -- within the assessment done by the -- by the PCPC's group that handles CIR -- handled the CIR process here.

Q. Okay. We received just before your deposition, a few days in advance, a list of materials that have been added to your reliance list since you produced your report in this case.

Did you provide that list of materials to counsel to -- are you aware of the materials that were identified?

A. Yes, I am. They're ones that I have reviewed since my report and -- yes, which would have been, I believed, important for you to know about, because obviously you wouldn't know if I hadn't provided that to you, and fair game for you to ask me about.

Q. On that list was contained a number of news articles.

A. Uh-huh.

Q. Are news articles pieces of scientific information that you typically consider in performing a risk assessment?

A. No, they're not part of my risk assessment, but they -- but they were

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relevant to -- they were relevant to my overall assessment of the issue of what the company is doing with regard to public dissemination of information.

So it's not the risk assessment part. It's more on the issue of the -- when I talk about the different influences of the company on public dissemination of information, I went through the different specific issues. So this would be a specific issue related to a news report that someone comes out with, the Reuters report, and then looking at what the company is saying in addition to that.

So it's understanding -- for example, the documents that Reuters discusses, many of those I'm sure I have seen, although I don't have access to -- I wasn't able to go on websites and download everything that they cite. But certainly they looked familiar, some of the ones I did see.

So it's that issue of -- the last part of my report, I think. Want me to tell you the section? It would be in the

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section on the role of the industry in Section 7.

Q. Okay. So the newspaper articles are not something that you are considering as part of your analysis of whether there is a risk of ovarian cancer from Johnson's baby powder, correct?

A. No, that's a separate issue because it's not -- it's not scientific data, per se.

Q. Okay. All right. Now, if you could turn to paragraph 31 in your report.

Okay. You discuss the biological effects of talc in this paragraph and in others, correct?

A. Yes, I would call this my introductory paragraph to transition into a specific topic, yes.

Q. Okay. And you talk here about the structure and size of talc affecting its properties.

What do you mean by that?

A. So whether it's fibrous enough, platy, fibrous. Whether it is particle sizes of less than 10 microns, less than 5 microns,

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greater than 75 microns. There's different -- certain pieces of literature deal with different size ranges of talc. The smaller the size range, the more toxic it is, for example, to lung tissue; the more likely it is to be able to move, based upon the size, versus being engulfed by a macrophage if it's a larger particle, things like that.

Q. So focusing specifically on ovarian cancer, what role does size and structure of a talc particle play with respect to a risk of ovarian cancer in your opinion?

A. I don't think I formed a opinion that it has to be a specific size or structure, because the -- my opinions are related to the fact that we have a complex mixture of ingredients within the body powder, and my assessment's been on the overall consumer product, not on any one particular ingredient only within it.

So it's the idea of just understanding that size and structure of these particles are general principles that affect toxicology. So a larger particle or a

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fibrous particle may have a different tissue toxicity response than a smaller particle.

So in other words -- I think I discuss this later in a paragraph about pleurodesis, the idea that you can get acute versus chronic inflammation, or respiratory distress or not. So it's just this idea of a general principle that outlines how you would think about particles generally as a toxicologist.

Q. Well, okay. So you said that your assessment is based on the overall consumer product. That would be Johnson's baby powder or SHOWER TO SHOWER®, correct?

A. Yes.

Q. All right.

A. Or Shimmer. I think that's the other name. There's a third product.

Q. Okay. But my question to you is, you actually cite a number of pieces of literature in the section about the alleged toxicity of talc that don't relate to the overall consumer products at issue in this case, correct?

MS. PARFITT: Objection. Form.

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THE WITNESS: No, I would disagree with that when you use the word "relate." Relate to me means is it relevant to the assessment, and they are, even if they're not just on the finished product.

But if what you mean is that there are studies that did not test the consumer product but individual ingredients or -- that is true, yes, but all of that is relevant or relates to the overall risk assessment.

QUESTIONS BY MS. BRANSCOME:

Q. Okay. So given your view that information about the individual constituents is relevant to evaluating the overall toxicity of the ultimate consumer products, then my question to you is: How does the structure and size of the component talc particles play a role in toxicity with respect to ovarian cancer?

A. Just generally -- it's not just -- well, with respect to ovarian cancer, we start with irritation, inflammation potential. Size of particles and shape are

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known to affect tissue toxicity as far as adverse events like inflammation and/or irritation.

Q. Okay. So that's -- that's what I'm trying to understand in more detail.

What is your opinion with respect to -- let's take size to start with. Is there a particular size talc particle that is more or less likely to cause inflammation, in your opinion?

A. It depends whether you're talking about acute or chronic. I would say for acute inflammation the larger particles, such as some of the particle sizes that are used in the pleurodesis products, are more likely to initiate an acute inflammatory response due to the fact that they're large enough that the body will recognize them with a fairly robust foreign body response.

Q. What is your definition of large?

A. So the literature varies, but certainly particles that are above -- some of the literature talks about particles that are in the range of 25 to 75. Some of them talk

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about larger particles even than that.

It has to do with the fact that -- this is complicated by the fact that any consumer product -- or any talc sample will have a range of sizes because they don't select for one size. They select for smaller than. So a 200 mesh, a 400 mesh, that has do with what will filter through.

So pleurodesis, they try to avoid for those products the really small -- large amounts of less than 10 because that leads to respiratory distress, whereas many of the consumer talc products are using much smaller, finer particles to get that feel and performance they want from the consumer body powders.

Q. Have you reviewed -- focusing specific on Johnson & Johnson's products, have you reviewed the documents that relate to the specifications for the Johnson's products with respect to the size of the plate particles?

A. I have seen those, yes. I can't tell you what each of them says without pulling them out, but, yes, that is certainly

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documents I have seen and relied upon.
Q. Is it consistent with your understanding that it was Johnson & Johnson's intention to select large platy talc particles for its products?
MS. PARFITT: Objection to form.
QUESTIONS BY MS. BRANSCOME:
Q. Have you seen that in the documents?
A. I don't know that it's described quite that way, but they certainly were doing a 200 mesh selection. So -- for their body powders products. So -- and they were trying -- and they did make attempts to look for sources that were more platy talc than other forms, but that doesn't ensure that everything is platy talc.
Q. Are you familiar with the term "fines"?
A. Yes, generally, but I'm not -- but I'm not an expert in the processing of talc as far as how you would go about choosing an ore or a mine. There's others that will be addressing that. That's not my

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area.
Q. What is your understanding of the term "fines"?
A. My understanding of the term "fines" has to be looking for a sample or a group that has been processed such that it has certain characteristics.
Other than that, I would refer you to the individuals in litigation that are going to be dealing with the processing.
Q. Okay. Have you taken into account in your analysis in any way the beneficiation process that occurs between the time that the talc is mined and it ends up in one of the consumer products that is relevant to your analysis?
MR. MEADOWS: Objection.
THE WITNESS: So what do you mean by taking it into account? Am I aware that they have something that's in place for that? Yes.
But take into account, what do you mean by that?
QUESTIONS BY MS. BRANSCOME:
Q. Are you familiar with the

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effects that beneficiation can have on the level of the component -- the components in talc and what ultimately ends up in one of Johnson & Johnson's consumer products?
MR. MEADOWS: Objection.
THE WITNESS: So I'm not -- I'm not familiar with all the details, but I am familiar that it is a process they're using to attempt to result in a product that has characteristics that would be desirable for a consumer product.
Again, there is my understanding that others are going to be discussing the geology or the processing, and that is not something I'm looking at.
The literature as it relates to what has been tested in the public literature in particular, and that would be either an ingredient or a -- or a consumer product or a -- they may discuss exposure occupationally to mining or milling, which is -- which is an issue that you can consider when

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you're reviewing that literature as well.
QUESTIONS BY MS. BRANSCOME:
Q. Okay. And so when you cite -- for example, you have a significant number of -- I'm trying to find the right paragraph.
You have a section in your report where you discuss a number of different articles that relate to talc, and in parentheses you identify that the talc source might be cosmetic, it might be industrial, things of that nature, correct?
A. Yes, I do that on purpose because I wanted -- I did look at the literature to understand what they were -- what they were -- what type of exposure they were describing.
Q. Okay. And so understanding that some of those products are not representative of what ultimately is in Johnson's baby powder, do you have anything in your report that explains how you did or did not give weight to those particular studies?
MS. PARFITT: Objection. Form.

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THE WITNESS: Let me look and see what I say.
If the question has to do with numerical rankings, no, I did not do that. But you're asking something else, right, broader than that, correct?
QUESTIONS BY MS. BRANSCOME:
Q. The question that I have is, how did -- is there somewhere in this report that I can understand the weight that you assigned to say a study that related to industrial talc as opposed to information about cosmetic talc, for example?
MR. MEADOWS: Objection.
THE WITNESS: So I -- I'm -- I believe I address that. I don't know it's exactly answering your question, but I lay out for you the characteristics of the literature in paragraph 37, and I point out that the scientific literature varies.
And the fact -- and I point -- and I admit -- I'm not admitting. I'm stating the fact that in some cases

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the authors will not describe it specifically as the type of talc, but just talc, whereas -- with no description of purity or state, for example. But in cases where the literature does, I did consider that in my weight of the evidence.
So, for example, when I -- when I lay it out here in these bullets where I'm putting for you tremolite mining industrial grade cosmetic, it certainly is something that I weighed. And obviously as much information as I can get on cosmetic-grade talc is going to be most important in the assessment, but that doesn't mean the other information isn't relevant.
You want me to explain why?
QUESTIONS BY MS. BRANSCOME:
Q. Well, so, for example, you describe the Dreessen article that related to trimellitic talc that's mined out of New York.
You would agree that trimellitic talc from New York is not

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something that ever ended up in Johnson's products, correct?
MR. MEADOWS: Objection.
THE WITNESS: I don't think I can answer that yes or no. I haven't done an assessment to see whether it ever ended up in the products. That's a different question.
I certainly am aware of the fact that was not a primary source of their talc, that is true. I do know that.
In other words, I don't have records from -- going back from 1894 on what the source of their talc was. So I can't tell you over time.
What I do know, what's been put into depositions and testimony of company employees more recently, where it's my understanding that the principal sources over the years were either the Vermont mine, the Italian mine or the Chinese mine. And there were different interruptions in time where different mines were used,

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depending on sourcing.
QUESTIONS BY MS. BRANSCOME:
Q. So as part of your expert analysis where you are evaluating articles that relate to different types of talc from different sources of talc, have you done an analysis of how those particular types of talc do or do not relate to what is in the consumer product manufactured by Johnson & Johnson?
MS. PARFITT: Objection. Form.
THE WITNESS: The first part of your question, again? I'm sorry.
MS. BRANSCOME: Would you read it back?
THE WITNESS: Could you read it back to me again? I didn't mean to wander, but the first few words I missed.
(Court Reporter read back question.)
THE WITNESS: Okay. So I certainly did, which is why I'm breaking this out here for you this way.

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So I am -- I am certainly recognizing, and I analyzed on the paper -- through the papers what type of product, if available, that the data is on.

But if you read my report in the process of risk assessment, all of these categories of papers are relevant to telling you something about what talc can do. And then when you talk about drawing final conclusions, I'm looking for information, if I can, and I have it, that is on point to the product that was sold.

So certainly the studies that give me information on cosmetic-grade talc are extremely important to my assessment, and they're ones that I've discussed or we've even used in trial before when we've talked about putting together a timeline.

That's what this is about, by the way. This discussion here, I'm starting to lay out what information

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was available over time, and that's simply what this is. It's a survey of the literature that talks about adverse effects of talc, and if I can, I separate it into different qualities or purities.

QUESTIONS BY MS. BRANSCOME:

Q. Dr. Plunkett, respectfully, I don't believe you answered my question.

Can you point me to anywhere in your expert report that's been produced in this MDL where you do an analysis of how the different talc types and sources that you are citing as support for the toxicity of talc generally relate to the products manufactured by Johnson & Johnson?

MR. MEADOWS: Objection.

THE WITNESS: So I don't know how else to answer that but to tell you I think that's what this whole section is about. I step you through -- I identify different types of evidence. I identify for you what was tested in those different pieces of evidence, and then I step through

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that to draw conclusions based upon what was available for me to assess.

QUESTIONS BY MS. BRANSCOME:

Q. Okay.

A. I don't know how else to answer it for you. That's what the section is meant to do, and that's why I broke it out that way. You know, I recognize that there is data on different things.

What's interesting about even the data on different things, there's a common mechanism that is involved with the type of tissue toxicity you get, and that's irritation and inflammation. Regardless of whether it is of a certain grade or not, you get certain types of adverse reactions. May be a more sustained reaction with a industrial grade versus cosmetic grade, but they all have the capability to produce that type of adverse effect.

Q. Dr. Plunkett, where can you point me to in your report that you discuss the weight that you give studies that relate to talc from New York as opposed to studies that relate to cosmetic talc that ultimately

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ended up in Johnson's baby powder?

MS. PARFITT: Objection. Form.

THE WITNESS: I've tried to answer that for you. The weight that I'm giving -- the weight that I'm giving is part of my assessment. So, again, I don't give numerical rankings. I've answered that for you. I don't do that.

What I instead do is I'm looking at everything that's relevant, everything that's available. I do categorize it, so I am selecting -- I am identifying or analyzing the information for what it describes. And then if you go further on down, I try to tell you what I think is important about that information.

The overall conclusions I'm drawing in the report, though, when I cite to specific studies in the risk assessment, the majority of those studies I believe that I'm citing for you, outside of notice, have to do with -- that's more of a warnings

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issue -- have to do with the issue of cosmetic talc. Because the human studies are describing cosmetic talc. The NTP studies is a pure talc. Many of the in vitro studies and other animal studies are looking at, quote/unquote, a talc that is not an industrial grade or from a mine that would have -- be looked at in that way. So --

QUESTIONS BY MS. BRANSCOME:

Q. You understand that there are different types of cosmetic talc, correct?

A. Yes, I am aware.

Q. And cosmetic talc can be mined from a number of different mines globally, correct?

A. That's correct.

Q. And some of the studies that you cite in your report are testing cosmetic talc from other consumer products, for example, Cashmere Bouquet, correct?

A. Some. The majority of them are not, but I would agree that some do, yes.

Q. Okay. Have you done an

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analysis of how the talc that is used in Cashmere Bouquet, for example, relates to the talc that is used in Johnson's baby powder?

Is that an analysis that you have done before relying on that information in your report?

MR. MEADOWS: Objection.

MS. PARFITT: Objection.

THE WITNESS: My analysis -- I did do an analysis to look at what was described, what products are described, but I certainly -- I certainly did not throw out studies that described Cashmere Bouquet because I would -- I still believe as a toxicologist and a risk assessor that those types of products are important to the overall weight of the evidence about the hazard and the risks posed by talc.

You know, I just -- I just -- I guess I disagree with you if you're saying they're irrelevant. I don't believe that they are.

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QUESTIONS BY MS. BRANSCOME:

Q. I was simply asking: Did you do an analysis that would allow you to compare the ingredients in another product, like consumer Cashmere Bouquet, before you rendered an opinion with respect to Johnson's baby powder based on tests of Cashmere Bouquet? Did you do that analysis?

MR. MEADOWS: Objection.

THE WITNESS: I do not have access to internal company documents for the manufacturers of Cashmere Bouquet, so I certainly couldn't do the analysis in the same way that I can do it here, where I can identify what Johnson & Johnson and Imerys describe as sources of the talc that was used for the Johnson & Johnson baby powder, without --

QUESTIONS BY MS. BRANSCOME:

Q. So you have no way of knowing one way or the other whether that talc is similar, correct?

MR. MEADOWS: Objection.

MS. PARFITT: Objection.

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THE WITNESS: Well, I think I do know it's similar, if you look on the bottle as far as what is described it being, but if you're asking me -- if you're asking did we fingerprint it to only a particular mine, this is the beauty of the data. The data shows that regardless of the type of product you're looking at, there's consistency across the study.

So -- but I did not try to segregate out studies that only dealt with Cashmere Bouquet, no, I did not do that.

QUESTIONS BY MS. BRANSCOME:

Q. Okay. As you sit here today as a toxicologist, is it your position that industrial-grade talc that might contain up to 70 percent tremolite presents the same level of toxic effect as cosmetic talc that may contain no tremolite or tremolite at a very, very low level?

MS. PARFITT: Objection. Form.

THE WITNESS: I haven't formed that opinion, no.

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QUESTIONS BY MS. BRANSCOME:
Q. Okay. And so have you formed an opinion that I could find in your report that discusses in any way the relative toxicity of different types of talc?
A. That, you may find. I need to go back and look how I set it out, but I think I -- I talked with you about the difference between fibrous versus platy. I do discuss that.
And I talk about the problems when you have a complex mixture that has added to it things like asbestos and heavy metals, because I talk about the additivity issue that can come to play. So that -- in other words, increased risk when you have a complex mixture with additional components that all share the same toxic properties as far as target organs or types of effects or mechanisms that are triggered in the body. That's what I point you to.
I -- I don't -- that's the only way I can answer that for you, I think, based on what I know I have in here.
Q. Okay. You talk about the term

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"asbestiform talc."
You talk about asbestiform talc.
Are you familiar with that?
A. I do mention that in my report, yes.
Where are you?
Q. At paragraph 30. It's on page 19 of your report.
A. Yes, I'm here.
Q. Okay. And the first sentence in paragraph 30 you state, "In the published medical literature, there is often discussion of talc using terms such as fibrous talc, asbestiform talc, non-asbestiform talc or tremolite."
Do you see that?
A. Yes, I do.
Q. Okay. Is it your opinion that tremolite is a form of talc?
A. So tremolite is a -- is a -- is a type of fiber or a -- tremolite is a -- is a substance or a entity that has been identified as a specific morphology, I guess, identified characteristics of a -- it has

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identified characteristics.
There's -- within the asbestos -- the asbestos literature there's -- it's one of the forms -- forms of asbestos that's described. For example, in IARC, they describe all of the ones that have carcinogenic properties. It's one of them.
Within the literature within Johnson & Johnson's documents, there's tremolite discussed as -- I assume them referring to asbestos tremolite, asbestos in a tremolite characteristic. I have seen tremolite talc also mentioned in the literature.
If you want a specific discussion of each of those, again, there's -- I understand there's experts that are going to describe the distinguishing characteristics of each of those.
I'm only setting out this is what I have seen, talked about, in the literature.
Q. So you are not an expert on the differences between fibrous talc, asbestiform talc, non-asbestiform talc and tremolite as

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it relates to toxicity. Is that your opinion today?
A. No, that's not what I'm saying. I'm saying that if you want me to -- I'm -- if you want me to describe the characteristics and the morphology of each of those individually, that's something a geologist would do.
But certainly as far as the toxicity assessment I did, each of these types of -- each of these words, I guess, or names have been applied in the literature when they talk about toxicity of talc. Some of the literature talks about fibrous talc or just -- other literature just talks about talc. Some of it, for example, the IARC monographs, distinguish between asbestiform talc and non-asbestiform talc in their assessments of the cancer risk.
And then tremolite is discussed as a component of talc. And I have seen papers that talk about tremolite -- nontremolite talc or tremolite-containing talc. That's how you most often see it.
So it's the idea that it is a

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constituent of certain mines that -- and that's my understanding of it. But if you want -- and they all -- they all certainly do show that the toxicity can be affected, whether it's a fiber or a platy particle. So tremolite being a fiber would certainly affect my overall assessment of risk. The more tremolite that you would have would make -- would make it more likely to be reactive in terms of a foreign body response, depending on the size.

Q. What's your basis for saying that?

A. That's based on a fibrous form versus a platy particle form. That's the issue of -- I have that paragraph where I talk about what macrophages look for, can engulf or not engulf. So those are all things that are important to a toxicologist to understand exist.

But certainly within my assessment I have to include literature from all of those because of the fact that all of those are relevant to the toxicity profile, since I know that the cosmetic baby powders

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and the data I've seen shows detection of something called fibrous talc.

I see detection of tremolite within certain samples of baby powder.

And then I have just the general category of asbestiform versus non-asbestiform when I consider the way, for example, IARC has reviewed the carcinogenicity.

So those are -- those are terms that I'm laying out because I think they are something you need to understand exists in the literature.

Q. Okay. But I'm trying to understand, not helping me understand the literature. I'm trying to understand your opinions with respect to toxicity.

Is it, for example, your opinion that fibrous talc has the same toxic potential -- let's focus specifically with respect to ovarian cancer -- as tremolite?

A. I haven't formed that opinion, but, again, I would -- my opinion has been formed on the fact that we have complex mixture that includes all of these things.

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Q. Okay. And so when you're looking at a complex mixture, you would agree as a toxicologist it would be important to understand the constituent elements of that mixture, correct?

A. Yes, it is important to understand that this is -- what is in the mixture, and that's -- that's part of what I try to do.

Q. Okay. And it would be important before drawing conclusions from one study that might have different constituent components, it's important to understand the relative toxicity of individual constituent elements, correct?

A. Depends if you can or not. I mean, there's certain types of studies you can, where in the published literature that's been described. That's why I'm pointing this out. It's the idea that within the literature, when you go through, it's important to understand what you can say about the consistency across the literature where maybe different types of talc are discussed.

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And that's what I -- I think I lay out for you. I tell you there's consistency in certain toxic effects that are seen. Regardless of the form that you're looking at, talc has certain properties, and all of these things are -- been shown to be in the complex mixture, so I have -- as a result, all of that literature has relevance to at least the hazard part of my assessment, and certainly have relevance to -- when you want to talk about warning and the final risk assessment, they're definitely relevant, but certainly the -- when I go through this process, I am trying to focus as much as I can on a product that is most similar to the one I'm assessing.

So obviously that's why -- that's one of the reasons I do look at the human data, because the human data is involving a consumer product use, which is what I'm talking about here.

Q. Is it using specifically Johnson's baby powder?

A. Many of them are, yes.

Q. Okay.

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A. Based on my understanding of what I see discussed within the literature.
Q. Did you identify in your report specifically which report -- which studies have used a consumer product manufactured by Johnson & Johnson?
A. I haven't laid them out individually, no, but I am aware of discussions of this general issue within some of the documents I've seen, and essentially Johnson's body powders products were the overwhelming share of the market.
Q. But you would agree that studies that did not involve the consumer product manufactured by Johnson & Johnson should be given less weight when analyzing whether or not there are risks associated specifically with Johnson & Johnson's products?
MS. PARFITT: Objection. Form.
MR. MEADOWS: Objection.
THE WITNESS: It depends on the question being asked within the assessment, the risk assessment. It really does, I mean, because each of

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these studies brings a piece of evidence to the risk assessment.
And so the question is -- for each one, you consider it on a case-by-case basis. It is possible, yes, that you would give less weight. It's also possible that you would not, dependent upon what you know about that study and how it relates to other studies that are out there.
QUESTIONS BY MS. BRANSCOME:
Q. So methodologically, how would I understand from your report marked as Exhibit 4 under what circumstances to give a study that relates to, for example, industrial talc less weight than a study that actually used Johnson's baby powder?
MR. MEADOWS: Objection.
THE WITNESS: Well, I've tried to tell you that. That's what I said for you. That's why I am doing it. I certainly am trying to focus in on studies that deal with the consumer product.
But what I find when I look

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across the studies that are dealing with not the consumer product but other descriptions, there is a consistency in the types of effects you see.
And since I'm not quantifying the risk but identifying it as being increased or not, in other words, is it more likely than not that someone exposed in this way could be at a risk of ovarian cancer, that's what I'm talking about.
So again, it's -- if I was trying to identify differences in cancer potency factors for different types, then, yes, if I had an animal study on each of those, I could compare potency for cancer, but that hasn't been done.
QUESTIONS BY MS. BRANSCOME:
Q. Okay.
A. So instead, what I have to do is rely on what is available to me. And based on my judgment, that's how I review the studies.

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Q. And so for the opinions that you are offering in the MDL, you agree that you are not quantifying the risk associated with Johnson's baby powder, SHOWER TO SHOWER® or Shimmer with respect to the potential for causing ovarian cancer?
MS. PARFITT: Objection. Form.
THE WITNESS: In terms of a cancer potency factor, that is true, I am not. Instead, what I am doing is I am quantifying whether or not I believe that the risk is increased above a background risk.
That has to do with -- that's where I bring in, in my risk assessment, the human data, because the human data is showing statistically significant increases in risk in populations using the consumer product.
So I have a quantification where I'm using the word "increased," and I believe to a reasonable degree of medical certainty that indeed the risk is increased. So I'm quantifying

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in that way, but I'm not giving it a number. I'm not saying that the cancer potency factor is such that you increase the risk from one in a million to 10 in a million to 1 in a thousand. That I have not done because I don't have the data, the studies. The company has not done studies on each of these to allow me to do that.

QUESTIONS BY MS. BRANSCOME:

Q. Okay. The reference that you made to the human data that you believe shows a statistically increased risk in populations using the consumer product, have -- which -- have you identified in your report which of those studies are specifically using a product that was manufactured by Johnson & Johnson?

A. I don't lay that out for my report, I do not, but certainly it is something that for some of the studies I believe you can -- you might be able to get some of that information from. But certainly I have not laid that out individually in my

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report, no.

Q. And you would agree that for some of those studies there is no information as to the specific type of consumer talc that the individuals who are being studied used, correct?

MS. PARFITT: Objection. Form.

THE WITNESS: I would agree that in some of those studies they're not saying, but that is why you look at the evidence overall.

And what's important to look at in terms of now -- if you wanted to go to Bradford Hill, that's why you look at things such as consistency. So what do the studies show. We see a certain level of increased risk across studies, regardless of who did the study or what population was being looked at.

So that's the best way I can answer that for you. That is -- that is part of the -- of the assessment that you look at.

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QUESTIONS BY MS. BRANSCOME:

Q. In reaching your opinion in the MDL that there is an increased risk above background of ovarian cancer from the use of products manufactured by Johnson & Johnson, have you made an attempt to identify specifically which studies, the human studies on which you rely, test or look at people who have used Johnson & Johnson's products?

MS. PARFITT: Objection. Form.

THE WITNESS: It's my -- my review of the study indicates that I would say for the vast majority of them you cannot do that.

But you can take what is reported and look at things such as market share and those kind of things to get an idea of what you believe the exposure would have been.

But certainly I have not -- I have not tried to apply some kind of a numerical value to how many people in the study may have used Johnson's baby powder or not, no, that has not been done. I don't think anybody -- any of

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the bodies that have looked at this have done that.

QUESTIONS BY MS. BRANSCOME:

Q. You have not done a market share analysis, correct?

A. No, I've seen this in documents only. I have not done my own. There are company documents that talk about their market share.

Q. Okay. Have you made an attempt to examine the levels of fibrous talc or asbestiform talc that are in different consumer products, aside from Johnson's baby powder or SHOWER TO SHOWER® or Shimmer?

A. So for that are you referring to things such as -- other types of cosmetics like foundations or lipsticks or --

Q. I'll rephrase.

Have you made any attempt to examine whether other cosmetic talc body powders have a different percentage of fibrous, or what you refer to as asbestiform talc, from the Johnson & Johnson products?

Have you done any analysis to make that comparison one way or the other?

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MS. PARFITT: Objection. Form.
THE WITNESS: I certainly haven't done -- I certainly didn't do a directed analysis to try to determine that, but there is information, I believe, in -- I think if you look at some of Dr. Longo's work, that may be there.
And I believe in Dr. Blount's published paper there may be a discussion of the type of powder product used, where she was looking for -- at least for asbestiform -- asbestos within the talc. It may be tremolite as well, but -- if you want me to look, I can do that. I just don't recall whether -- I think she did talk about sources of the talc, where it came from, so...
QUESTIONS BY MS. BRANSCOME:
Q. Okay. But as you sit here today, you can't point me to any analysis that you did or an analysis that you relied on that would relate different brands of cosmetic talc body powders with respect to

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their constituent components?
MS. PARFITT: Objection. Completely misstates her testimony. She mentioned Dr. Blount. She mentioned others.
THE WITNESS: So I think what I started with, I said I haven't done a directed analysis to try to determine specifically how this product versus this product versus this product may have looked over time, because I don't have access to a full data to do that.
But what I do have is data that has -- I do see published data, for example, Blount and maybe some of the other published studies, that looked at this issue, at least of asbestos presence in talc. And I believe Dr. Longo also had things that weren't just Johnson's. I believe he had Cashmere Bouquet, for example, samples in some of the things he looked at.
So I can point you to those things that I have reviewed, but I haven't -- there's nowhere in here

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that I state for you that it's my opinion that Cashmere Bouquet has this specific pattern of constituents as compared to Johnson & Johnson's. No, I have not done that.
QUESTIONS BY MS. BRANSCOME:
Q. Okay. And that would be true for any other brand of cosmetic talc, body powders, Jean Nate, Lily of the Valley, not just Cashmere Bouquet, correct?
MS. PARFITT: Objection.
THE WITNESS: That is correct, I don't have access to that information.
QUESTIONS BY MS. BRANSCOME:
Q. Have you done any analysis of the constituent components of talc and how they have changed even within Johnson's -- Johnson & Johnson's manufactured products, how the constituents of the consumer products may or may not have changed over time?
A. I've done some of that, yes, and I laid that out, I think, for you, when I talk about the differences in the products that are described within the documents, the

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company documents, from the '70s versus the '80s versus later on, as far as the changes that were made to specifications of the product, for example. That's something -- and I think I've talked about that a bit at trial as well.
Q. Okay. And is it your view that the risk potential for Johnson & Johnson's manufactured products have changed at all over time with respect to ovarian cancer?
MS. PARFITT: Objection.
THE WITNESS: I have not -- I have not attempted to differentiate a risk potential at only one point in time.
What I have done over points of time is looked at the issue of warnings and what should be warned about.
But my analysis related to the hazard or the risk assessment of the products is considering all of the available information, which would be all of that information over time.

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QUESTIONS BY MS. BRANSCOME:
Q. Okay. You talk about, in paragraph 35 primarily -- we'll talk about the fragrance components in more detail, but you talk about the idea of chemicals being a potential irritant.
Are you familiar with that?
A. Yes, that's correct.
Q. Is it your position that any product that contains chemicals that could be an irritant should be labeled with a health warning?
MS. PARFITT: Objection.
MR. MEADOWS: Okay.
THE WITNESS: I don't think that's -- no, I don't think I've formed that specific opinion.
But the opinion that I think I'm expressing here is that when you have a -- the information that I have, which unfortunately the company hasn't given us percentages or actual levels, instead, what I do as a toxicologist, I look at what is there. And when I see over a hundred chemicals there,

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that 70 percent of them have been linked as an irritant hazard, there is the issue of toxicological additivity to consider.
So certainly as a risk assessor, when I have that many potential sources of irritation as far as chemicals going into a complex mixture, certainly I think I have formed the opinion that I think that is something that needs to be considered when you're talking about providing information to consumers, yes.
QUESTIONS BY MS. BRANSCOME:
Q. As a toxicologist, would it be important to you to understand the exact percentages of all of the constituent components of, say, Johnson's baby powder, for example?
A. Are you talking about just the fragrance or are you talking about everything that's in it?
Q. Dr. Plunkett, you referenced the fact that the company has not provided

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you with specific percentages, and so I'm asking you, is that something that as a toxicologist would be important information to you?
A. Depends. Certainly with the fragrance -- and I'm talking about the conversation about this paragraph is focusing on the fragrance components.
So, yes, I mention that it would be nice to know, it would be good to know, if we could, exactly what was in there, because I could quantify the hazard or quantify the risk, actually. So instead, I have -- I identify it as a hazard, but I can't quantify it without those levels.
But does that change -- make a difference in the overall conclusions I draw? No, it doesn't affect the overall conclusions that I have drawn, but it adds that other piece of the puzzle that deals with the fact that we have a complex mixture that have a combination of ingredients that target irritation.
And irritation and the potential to produce an inflammatory

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response, in my -- if you've read my report, you understand that I think that's a key factor in increasing the risk for ovarian cancer.
Q. Understanding the percentages of the constituent components, is that limited only to fragrance, or would it also be important to understand the percentages for the heavy metals that you contend are in Johnson's baby powder?
A. So if I was trying to define the hazard of each component, I would certainly want one to know that. As a result, what I'm doing instead is looking at the complex mixture. In other words, this is a mixture of all these things.
I break out those individual components, or constituents, to tell you about the hazard that is brought to play or the toxicity profiles that exists. And what's important about that in my overall evaluation of the end product, which is what my risk assessment is based on, the end product, shows that I have multiple components with similar types of effects.

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And as a toxicologist, when you do that, that affects the conclusion that you can draw about a body of literature.

Q. Okay. You do understand that there is testing data available about the percentages of the constituent components with respect to heavy metals, et cetera, that have been in Johnson's baby powder over time, correct?

A. There is some information. Unfortunately, the information is not complete as to every lot or every sample, as far as what I have seen. And also, there's some -- some of the sampling is reported as more of a limit versus an actual quantification. So it depends upon which -- which result, study result or document, you're looking at.

There is some there, yes, and that's one of the reasons why I identified these as part of my risk assessment, because I look for a pattern of these metals that are known to carry a hazard and whether or not these are ones I'm seeing detected time and time again.

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Q. But you made no attempt to quantify the risk with respect to any of those components or use that data in any way, correct?

MS. PARFITT: Objection. Form.

THE WITNESS: No, I used that -- that data as part of -- my risk assessment as part of my hazard assessment, absolutely. It's part of the hazard assessment.

But as far as quantifying them individually, no. I am quantifying the risk and looking at the risk of the entire product, not of just one individual component of the product.

QUESTIONS BY MS. BRANSCOME:

Q. Well, we already discussed you're not quantifying the risk with respect to the entire product, correct?

A. Well, I'm quantifying it in terms of an increase above background, which I'm not giving you a -- I told you I wasn't giving you a cancer potency factor. That is true. That I am not doing.

But I am quantifying it by

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using a word such as an increase -- an increased risk.

Is that a specific number? Am I telling you that it's increased by two times or four times or six times? No. The data available did not allow us to do that, with the exception of the epidemiological data. And the epidemiological data can show you that in that piece of evidence there appears to be a 30 percent increased risk above background.

Q. Did you make an attempt to quantify the risk with the data that you had available to you with respect to the final consumer product?

A. I could not, based on the data I had, because I didn't have a well-controlled animal study to be able to pull that out that way.

Instead, what I -- in this type of weight of the evidence, you look at what you might be able to quantify based on the human data. And certainly the human data showing the statistically significant consistent findings across studies for that

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30 percent increased risk, that is part of my overall weight of the evidence for me making the statement the risk is increased.

But you'll notice I don't say increased risk of 30 percent, because I don't believe that I can state that with certainty in the way I do a risk assessment. But certainly as any one individual -- any one individual piece of evidence or any one body, like the epi data, others have made -- other bodies who have looked at the -- talked about the consistency of the increased risk signal in the epi studies as being in the range of 30 percent.

Q. Okay. But you would agree that based on the methodology that you applied in this case, you could not say to a reasonable degree of scientific certainty that there is an increased risk of, for example, 30 percent with respect to use of Johnson's baby powder and ovarian cancer, correct?

MR. MEADOWS: Objection.

THE WITNESS: I have not done that. And I'm not saying that somebody else couldn't do that. I

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have not -- I have not chosen to do that based on my evaluation of the data.
QUESTIONS BY MS. BRANSCOME:
Q. And the same would be true if I asked that question and substituted any particular number, a 10 percent increased risk, a 20 percent increased risk, correct?
MR. MEADOWS: Objection.
THE WITNESS: I haven't given a specific number in my final opinions, that is true.
QUESTIONS BY MS. BRANSCOME:
Q. Okay.
A. I've tried to explain to you what evidence I do think is there, however.
Q. Now, we've talked about different types of talc that might have different constituent components, but you also look at exposure to talc in an occupational setting.
Do you recall that?
A. Some of the studies that I've relied upon, yes, some of them were occupational.

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Q. Okay. And you understand that in an occupational setting, you would agree that the exposure, particularly via inhalation, would be much higher than it would be through the use of a consumer product, correct?
A. It depends on the occupation, but, yes. For example, I would agree a miner would be expected to have that, but there are certain, quote/unquote, occupational studies where the exposure levels that -- for example, there are -- I believe there's at least one study that looked at application of talc powders in -- maybe in a material, coating materials in a factory. Those kinds of studies would be different than a mining study.
But, certainly, yes, I understand that occupational studies, the inhalation exposure is the pathway that would be predominant versus in the consumer body powder use, I'm talking about the predominant exposure pathway in my opinion is going to be through perineal use, even though inhalation exposure can occur.

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Q. Is it your opinion as you sit here today that someone could develop ovarian cancer through -- exclusively through the inhalation of Johnson's baby powder?
MS. PARFITT: Objection.
THE WITNESS: I haven't formed that opinion at this point in time.
QUESTIONS BY MS. BRANSCOME:
Q. Have you done any analysis or can you point me to any analysis in your report that makes a comparison of the exposure levels that might be seen in an occupational setting to what would be seen by a consumer?
A. Are you asking me for a piece of evidence that does that comparison, or is there evidence that allows you to do that comparison?
Q. Have you cited or discussed any of the evidence or done an analysis in any way that would compare exposure levels in an occupational setting to what you would anticipate a consumer using Johnson's baby powder might be exposed to?
A. I don't think I did it as a

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separate analysis, but as part of my analysis I considered evidence that showed -- provided me with such data. So, for example, if you want, I can point you to a -- I have an inhalation paragraph, I think.
Let me look for it real quick. See if I can find it quickly for you. I don't want to waste your time.
Q. Sure.
A. So there's -- I don't see it cited here, but there's at least one document I reviewed where the company themselves made a comparison, and I have seen that, of inhalation exposure to talc suspended in air with diapering. Dr. Longo has done a measurement of exposure in air with perineal application of talc. So I'm aware of those studies.
And then I certainly am aware of the fact that those numbers are different, or smaller, than many of the numbers I see reported in some of the occupational studies. But I can't say that's true for all.
I would certainly, though, say that if you're just talking inhalation, I

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certainly would expect a miner or a miller to have a greater potential for inhalation exposure than routine use of the consumer product, with the exception of the studies -- the reports of large amounts of exposure in children where the inhalation -- where they were inhaling large amounts of powder.

And so that's a different story. That's sort of an acute overdose exposure, I guess, versus the typical daily exposure through occupational or consumer use.

Q. And that raises an interesting question. You discuss health hazards associated with talc being known, and in some cases deaths had been reported.

You're aware that those relate to asphyxiation deaths, correct?

A. Or long-term injury to lungs. Maybe not an immediate asphyxiation, but lung damage produced by large amounts -- some of the children would go to the hospital and be sick for a while and then die. So they didn't asphyxiate immediately, right? But some of them did. You're exactly right.

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Both of those things occur, and I address that also in my warning section about the fact that that warning didn't -- was not put on the product for a long period of time even though those types of reports were coming in early.

Q. You would agree that that is a completely different biologic mechanism than what you are proposing the biological mechanism is for ovarian cancer to develop with respect to talc use, correct?

MR. MEADOWS: Objection.

THE WITNESS: I would agree that it's an acute response versus chronic, yes, that I agree with.

It's not entirely different in some cases because some of the tissue reactions you saw were indicative of irritation when some of the lung samples were looked at. But certainly, yes, that's acute exposure versus chronic exposure, and I'm focusing on ovarian cancer on chronic exposure scenarios.

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QUESTIONS BY MS. BRANSCOME:

Q. Okay. Now, you would agree that -- so let's set aside inhalation.

You agree that for talc -- for Johnson's baby powder or another one of Johnson & Johnson's consumer talc products to reach an individual's ovaries, it must pass from the perineum, through the vagina and the cervical canal, move across the uterus -- and again, it's the ciliary motion of the fallopian tubes -- cross the peritoneal space between the fimbriae and ovaries, escape phagocytosis in the peritoneal space, and then attach to the surface of the ovaries, correct?

MS. PARFITT: Objection. Form.

MR. MEADOWS: Okay.

THE WITNESS: If the issue is attaching to the surface, yes. There's also some information indicates the site of attack may be actually at the fallopian tube exit to the peritoneum. But, yes, that's correct, there's been some discussion in the literature on ovarian cancer

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about whether the tumors are arising in the tubes versus the ovaries.

But I would agree, I think both -- I think both of those things -- those things -- there is a passage that has to happen, regardless of whether the end point is at the fallopian tube or at the ovary.

QUESTIONS BY MS. BRANSCOME:

Q. Okay. Is it your view that the consensus has been reached that ovarian cancer can be caused by talc landing in the fallopian tubes?

A. I haven't formed that opinion, though I do believe this will be discussed by some of the other experts.

Q. Okay. Have you personally conducted any tests or experiments to confirm the theory that talc migrates from application at the perineum to the ovaries?

A. If by that you mean something where I performed a laboratory test myself, no, I have not done that.

Q. As a toxicologist, are you capable of doing that?

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A. Yes, I believe if asked I could -- I could attempt to design something to look at that issue.
Q. Okay.
A. But I would argue that I think it doesn't make a lot of sense to revisit based upon what we already know from the scientific literature and the review papers from the gynecological community. I believe it's -- it's understood that it can migrate.
Q. In your opinion, has an animal model been successfully developed that would allow the testing of talc migration in humans from the perineum to the ovaries?
A. I think I tell that you in my report. I believe that the human data is the relevant data to look at this issue.
So it would be very difficult to design a study to do this based on the typical laboratory species that are used in toxicology testing. Even -- even the monkeys have issues, and the biggest issues with monkeys is the ethicality of using a monkey to settle -- to address a question that I believe is settled within the gynecological

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and scientific community.
Q. Now, you state in your report that talc that's applied through perineal use -- I believe the term you use -- routinely migrates to the ovaries.
Is that your opinion?
A. Are you reading from my report?
MR. MEADOWS: To the extent that question is still lingering, I object to it.
QUESTIONS BY MS. BRANSCOME:
Q. On paragraph 43 on page 29.
A. So I think as I've stated it, the studies that I have reviewed demonstrate that inert particles routinely move from the lower female reproductive tract up into fallopian tubes and towards the ovaries.
Q. What do you mean by routinely?
A. It's the percentages of movement that are reported in the patients. In other words, if you look at some of the individual studies -- if you want we can pull them out, but, you know, eight of ten patients, nine of ten patients, all the patients showed movement of the particles.

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And then on top of that, you have the review articles that talk about migration of particles in the female reproductive tract and are describing it as an event that is known to occur. So it's those things weighed together.
But certainly routine could be supported by the observations where the majority of the patients in the studies were showing movement of inert particles.
Q. Is it your opinion that every perineal application of cosmetic talc powder results in talc being deposited on the ovaries?
A. I have not formed that opinion, no.
Q. Have you formed an opinion as to with what frequency -- so let's say someone uses a cosmetic talc on a perineal application ten times. Out of those ten times, have you formed an opinion as to how many of those instances would talc deposit on the ovaries?
MS. PARFITT: Objection.
THE WITNESS: I haven't formed

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an opinion in that particular way, no. I think what I've -- I've tried to describe to you in my report is that I believe it is known that inert particles have the ability to migrate. And based on that, I form the opinion that it's my opinion to a reasonable degree of scientific certainty, which would be a more likely than not standard, that particles of talc would be migrating when women are using them perineally. But I haven't told you that it has to be a specific number, no.
QUESTIONS BY MS. BRANSCOME:
Q. Have you done any analysis to establish over a lifetime use of cosmetic talc where the app -- the perineal application, with what frequency during a lifetime the talc may have been deposited on that individual's ovaries?
A. So I certainly looked for information to allow me to assess that, but unfortunately those kinds of studies would be unethical to do. Because that would be a

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matter of sampling women during -- using them and then taking biopsies, and that's something that would be difficult to do. I would say impossible to get approval to do under human testing guidelines.

Q. Okay. So it's your opinion that it is possible for talc that is applied through a perineal application to reach the ovaries, but you cannot say with what frequency that occurs?

MS. PARFITT: Objection. Form. Misstates her testimony.

THE WITNESS: That's not -- what I'm telling you is, I think it -- that to a reasonable degree of scientific certainty that it migrates, and that would be the standard of more likely than not. I think it's more likely than not that the talc is reaching the ovaries when people are using it perineally.

I did form the opinion -- and I've talked about this at trial and yesterday. I have formed the opinion that this is a issue of chronic or --

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or use of the products. In other words, people aren't just using it once, but people are using it -- you can use the word "routinely," as a habit, in their daily life perineally. And that would be consistent with the studies that have been done that have looked at the issue of dose response.

And I discuss that in my report, too.

QUESTIONS BY MS. BRANSCOME:

Q. Okay. But you have not made an attempt to quantify, nor have you seen it in the literature, the overall dose of talc that someone might be exposed to in terms of contact with the ovaries throughout their lifetime, chronic use of cosmetic talc?

MS. PARFITT: Objection. Form.

THE WITNESS: Those -- that's the kinds of studies that have not been done and I believe could not be done based upon ethics of human testing. But certainly I -- that -- that data is not available that I'm aware of.

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MS. BRANSCOME: Okay. Can we just go off the record for a second?

VIDEOGRAPHER: We are going off the record at 12:23 p.m.

(Off the record at 12:23 p.m.)

VIDEOGRAPHER: We are back on the record at 12:24 p.m.

QUESTIONS BY MS. BRANSCOME:

Q. As you sit here today, how would you characterize the biological mechanism by which you claim Johnson's baby powder, their other cosmetic talc products, present a risk of ovarian cancer?

A. So I outline this for you in the MDL report. I think I have a section on -- let's see if I can -- you want me to tell you where or...

So paragraph 65, I think I set out part of this argument or part of this. And then also in paragraph -- I believe in 67.

Q. All right. Well, let me take a step back.

Is it your opinion that the biological mechanism by which talc, cosmetic

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talc, can in your view cause ovarian cancer, is that something that has been definitively established?

A. What do you mean by definitively? I mean, I think -- I believe more likely than not that -- so I believe I have reached a conclusion that I think what the most likely biologically plausible mechanism, but maybe you're ask -- meaning something else.

Q. Okay. Well, let's start with specifically you discuss a number of different potential mechanisms in your report. So if you believe you have reached an opinion more likely than not about the specific biological mechanism by which cosmetic talc and specifically Johnson & Johnson's products can cause ovarian cancer, can you describe that for me?

A. So it's a chronic inflammatory process, and so -- but like all compounds, constituents, even drugs that we look at, we don't know each individual step within the molecular mechanism.

Instead, what we know is that

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there are certain components to the process of cancer that are consistent with the effects produced by talc, and we know that talc can produce a chronic inflammatory process.

And so that's why I was pointing you to the paragraph 65 and I think 67.

Q. Is it your opinion that consensus has been reached in the scientific community that cosmetic talc can cause ovarian cancer through a chronic inflammatory response?

MS. PARFITT: Objection.

THE WITNESS: I don't know that that's exactly the opinion I've formed.

Would you like me to -- I could restate what I believe, but I don't think that's exactly how I would state it, no.

QUESTIONS BY MS. BRANSCOME:

Q. Okay. So then yes or no: Has consensus been reached in the scientific community that cosmetic talc can cause

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ovarian cancer through a chronic inflammatory process?

A. I don't believe I formed the opinion either way, that it's yes or no, because I haven't tried to -- I haven't tried to form the opinion about what the -- in other words, I haven't -- I can't say for every scientist out there.

I certainly can tell you what I believe based on what the consensus of science says about mechanisms underlying cancer and the consistency of those mechanisms with talc, and then I have an opinion about what I believe that information says.

I do believe my opinions, however, are consistent with some consensus statements, such as the issue on the mechanism is consistent with consensus opinion reached by IARC, where they discuss the inflammatory process as an underlying biologically plausible mechanism that can lead to ovarian cancer.

I think it's consistent with the Canadian risk assessment where they

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discuss those issues.

I think it's consistent with -- I don't know if the ACOG statement goes that far on mechanism, but it does talk about ovarian cancer. That's a recent statement.

And I believe it's consistent with some of the -- I believe my opinions are consistent with some of the opinions reached by others in science, but that's the only way I can answer that for you.

Q. Okay. Because you have not, one way or the other, done an evaluation of whether or not chronic inflammatory process is a biological mechanism on which the scientific community has reached general consensus with respect to the causation of ovarian cancer; is that correct?

MR. MEADOWS: Objection.

THE WITNESS: I can't tell you that -- I can't tell you that every body that's looked at it, but I have tried to point you to evidence that I believe is consistent with that.

For example, the IARC would be a good example of consensus on

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biologic mechanism because they have a whole part of their assessment of non-asbestiform talc and perineal cancer -- of perineal use and ovarian cancer that discusses mechanism. And that is consistent with what I have said. So there is a consensus opinion.

But I guess what I'm saying to you is I can't tell you that all -- all people who have put statements have come to that exact opinion. But there aren't that many places out there that are addressing that issue as far as the consensus on a mechanism. There's more statements about the relationship between ovarian cancer and talc use than there are drilling down to what the mechanism must be.

QUESTIONS BY MS. BRANSCOME:

Q. Okay.

A. So that's the issue. It's a little -- it's a little hard to answer that yes or no because of that.

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Q. Okay. When we talk about the idea of biologic -- a biologically plausible mechanism, what is your understanding of the term "plausible" in that expression?
A. When I use the word "biologically plausible mechanism" or "biologic plausibility," I'm using it consistent with what Bradford Hill uses, that's it's the idea that the evidence that available makes -- the evidence that available supports a pathway where you can go to exposure to response.
So in other words, there's a -- the biological information is consistent with how we know cancer can develop. That's the response we're looking at. And the exposure we're looking at is known to produce those kind of biologic events.
So as a result, based upon knowing that there's a consistency between the data that we have on the -- on the exposure and the data that we have on the way cancer can occur, those things -- those things align. So that makes it biologically plausible that that could occur.

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Q. But you would agree that biological plausibility suggests that it is a plausible explanation, but it may not have been established as the definitive pathway by which a disease is caused, correct?
MS. PARFITT: Objection. Form.
THE WITNESS: Well, I would agree that in the discussion of biologic plausibility in the Bradford Hill paper that is true. But if you look at people's discussion of the use of -- I want to say "biological mechanism" rather than the word "biologic plausibility," because really as a toxicologist I'm trying to understand whether there's a biologic mechanism that makes sense. Those are words I like to use. Does it make sense that this exposure could lead to this response.
And that involved looking at the mechanistic data or the data on the way toxic responses are produced by talc, and whether or not they align with the types of toxic insults that

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are known to be able to produce, specifically, ovarian cancer.
QUESTIONS BY MS. BRANSCOME:
Q. Is it your opinion that IARC, for example, has concluded that the biological mechanism by which talc may cause ovarian cancer is chronic inflammation?
MS. PARFITT: Objection.
THE WITNESS: I don't know that they have used -- they've described it quite that way, but they do describe what they believe is the biologically plausible mechanism. Because they do organize and use within the definitions of how they describe some things that are consistent with what Bradford Hill uses.
QUESTIONS BY MS. BRANSCOME:
Q. Okay. And obviously you're familiar with the IARC evaluation of talc with respect to the possibility of causing ovarian cancer, correct?
A. Yeah. If you mean the recent one, yes, the most recent assessment.
Q. Yes.

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And that IARC has in fact classified cosmetic talc not containing asbestos as possibly carcinogenic to humans, correct?
A. It's a possible human carcinogen 2B, that's correct.
Q. Okay. And if a product is listed in the 2B category, does that necessarily mean the product, in your view, is carcinogenic?
A. Not always, because that comes down to an assessment of -- then you're putting together a -- a risk assessment that looks at -- looks at -- across the information that you have available. And that may be that -- that the -- the possible is all you can say, or it may be that you believe that the information -- there's enough information there to take it further.
Has a possibility -- that's what I said, they do a hazard assessment. They rank things on hazard based on -- on unlikely -- not enough evidence, less -- the possibility, the probability or it's known.
Q. In your opinion, is your

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characterization of the risk of Johnson's baby powder or talcum powder products with respect to ovarian cancer, are you in the MDL characterizing that risk as a higher level of risk than what IARC characterized it, or do you agree with the 2B characterization of possibly carcinogenic?

MS. PARFITT: Objection. Form.

THE WITNESS: So I'm not IARC, so I don't try to second-guess there. They have reached a conclusion, and I use that as part of my weight of the evidence. So I haven't formed the opinion they're right or wrong.

But I have done a different assessment. My assessment, first off, includes more information than IARC had, so as a result, I have formed the conclusion that I believe that it's more likely than not that exposure to -- perineal exposure to talc body powders increases the risk of ovarian cancer in women who use that product.

And I will put the caveat this has to be chronic use or repeated use,

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because I've gone -- I've said that many times.

So that -- that is my opinion. So that's a different statement and a different assessment than what IARC does.

But -- so I don't disagree with their possible -- I weigh that, but I believe the evidence for the risk assessment shows me that it's more likely than not that this -- this exposure will increase the risk above a background risk for women who are using this product.

QUESTIONS BY MS. BRANSCOME:

Q. And how do you define chronic or repeated use?

A. Well, that is variable within the literature. For me, chronic is exposure -- if as a toxicologist, I would typically say chronic use is years of use. It doesn't have to be daily, but it would be years. That's the most common description you see in toxicology, so I would say that's fair. That's a fair assessment of my

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opinion.

Q. Is there a threshold of the use of Johnson & Johnson's talcum powder products below which there is no increased risk, in your opinion, of ovarian cancer?

A. We have not identified that threshold. That's what's missing within the -- the literature that exists today. So I can't tell you whether or not with only a thousand applications over a lifetime that is -- is not enough for every individual or not, but certainly I do believe that the -- that the exposure has to be habit, routine, chronic, something that is done maybe not on a daily basis but on a routine basis in a woman's life.

So that is consistent, I think, with the literature.

MS. BRANSCOME: Okay. We can go off the record.

VIDEOGRAPHER: We are going off the record at 12:36 p.m.

(Off the record at 12:36 p.m.)

VIDEOGRAPHER: We are back on the record at 1:35 p.m.

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QUESTIONS BY MS. BRANSCOME:

Q. Good afternoon again, Dr. Plunkett.

A. Good afternoon.

Q. I want to talk a little bit about the Health Canada assessment.

We talked about this before, but this is something that you reviewed after you completed your report which has been marked as Exhibit 4, correct?

A. Yes, and I wanted to tell you, I did not bring all those documents printed. I apologize. So there is a separate Health Canada draft risk assessment that I didn't print.

Q. Okay. So when you're referring to the Health Canada analysis, what document are you specifically referring to?

A. So I'm referring to the -- the combined documents, but there are times when you've asked me questions that I've been referring -- and I tried to say, I believe, Taher.

But, yes, some of the questions you asked me when I said Health Canada, I was

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talking about the combined documents, which would include their -- I guess it's called a draft risk assessment document, yeah, which refers to this document but is a separate -- is their own separate statement.

Q. As you sit here today, what is your understanding of the current position that has been articulated in the collection of documents that you refer to as Health Canada with respect to any potential relationship between cosmetic talc and ovarian cancer?

A. So that's why I did print out the small one, because I think it summarized it. So here, if you look at this Exhibit 6, it makes specific conclusions or draws -- makes statements. And essentially it talks about talc being a possible risk of ovarian cancer, but then it gives women specific advice about what to do in order to minimize exposure to the products, and some of that was relevant as well.

Just one reason I printed it out, it has to do with either choosing an alternative product or avoiding genital

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exposure to talc.

And let me see the exact words that they use, but --

Q. Before you do that, do you agree with the characterization that cosmetic talc presents a possible risk of ovarian cancer?

A. No, I don't think that's my opinion. I think my opinion is stronger than that.

But are you talking about my causation analysis opinion or just my risk assessment opinion?

Q. I'm asking about any opinion you intend to offer in the MDL.

A. Okay. So I will not be giving the causation analysis opinion, so that -- I will take that off the table.

So I think my opinion is a little stronger because I say that the exposure to the perineal -- the talc by perineal application in women increases the risk. So I'm not saying it's a possible risk. I'm actually -- I believe that it increases the risk. And I do believe that

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there is a association between those two things, the exposure and the response, which is more than a possible association, if you want to use those words.

But my assessment that I've done is not exactly the same, for example, as IARC does, which is more of just a hazard assessment.

Q. Right.

So I'm focusing my questions now on your risk assessment as compared to the documents that you've supplied us with with respect to Health Canada. And if I understand it correctly, are you stating that your opinion with respect to the relationship between cosmetic talc and ovarian cancer, you believe that it is an association that is stronger than a possible risk; is that correct?

A. Well, I don't say it's a possible risk; I say there is an increased risk. So I think it's a different statement, yes, absolutely.

Of course, I'm not Health Canada, so, you know, they have a framework

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upon which they make decisions, and I'm doing an analysis based on what I have done. And so it's not exactly the same, although some of the same documents and information is weighed within -- and then that's when you have the issue of what Health Canada does versus what they rely upon.

But this Taher risk assessment is just one piece of information that Health Canada has weighed in their assessment if you read their -- their draft risk assessment.

Q. So the question I have about the Taher risk assessment, earlier you were referring to the fact that you have only seen a quantitative assessment of the weight of particular components of scientific evidence in evaluating epidemiological studies; is that correct?

A. So that's what I typically see, yes. And I don't know that -- I've never seen it. But the typical approach would be to use it there as opposed to using it in the context of a human health risk assessment based on animal in vitro data.

Q. All right. Are you familiar

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with something called the Klimisch scoring system?
A. I don't know if I am now. You'll need to show me what it is you're referring to. The name doesn't ring a bell, no.
Q. Okay. So it's not something that you've used in the past?
A. No, not that I recall using.
Q. All right.
A. Unless it has another name, and that's why I'm asking you.
Q. All right. So if you have actually -- it's the document in front of you that we've already marked as Deposition Exhibit 5, I believe.
A. Yes.
Q. And that is the Taher study that we were discussing and is cited by the Health Canada risk assessment.
If you turn to page 5 -- well, actually beginning on page 4, do you see there is a section entitled "Literature Search and Identification of Relevant Nonhuman Studies"?

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Do you see that?
A. Yes.
Q. And this is related to an analysis that these authors performed on potentially relevant animal and in vitro studies, correct?
A. Yes, that is true.
Q. All right. And it states here that "all retrieved studies were examined for relevance, reliability and overall quality using the Klimisch scoring system."
Do you see that?
A. Yes, I do see that. So I have seen that before. I just didn't -- I didn't recall it.
Q. Okay. And so would you agree that it is possible and in fact has been done in a study that you rely on to apply a quantitative scoring system to animal and in vitro studies, particularly in the context of looking at the relationship between talc and ovarian cancer?
A. Well, I didn't say it was impossible. I said I don't believe it's routine based on my experience.

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So, yes, if they stated they've done -- we'd have to pull the supplementary materials out, but I recall them doing scoring based on epi studies but not on the -- all of the animal studies that they talk about. But we can pull it out and look. I could be wrong.
Q. Okay. Did you review the supplementary material 7, 8 and 9?
A. Yes, I did, and we'd have to pull them out because I don't recall the details.
Q. All right. We may take a look at those in a minute.
It talks about them classifying the animal and in vitro studies into four categories of reliability.
Do you see that?
A. Yes.
Q. So did you make any attempt, when you were reviewing the various studies in reaching your opinion about the potential risk of talc in causing ovarian cancer, did you make any attempt to separate out the different pieces of evidence into categories

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of reliability like the authors of this paper have done?
A. I didn't do it exactly the way they did it, but I certainly do do that as part of my screening.
I told you one of the characteristics or one of the assessments I make is whether I believe the data is reliable data that I can -- that I can use in a weight of the evidence. So I make a -- and when I talk about reliability, I'm talking then about things such as I mentioned, peer review, whether or not there is statistical analysis, whether or not the study is designed in a way that's consistent with general principles of toxicology, control groups or not control groups.
Those kinds of things I do -- I do consider when I am assessing the use of a study or not.
Q. Is it your testimony here today that contained within your report that's marked as Exhibit 4, I could find categorization of reliability of each of the pieces of scientific literature that you have

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included in your weight of the evidence analysis? Is that your testimony today?
A. No, that's not what I'm telling you, no.
Q. Okay. So you would agree that you did not -- first of all, did you develop categories of reliability in which you separated the particular scientific studies into as part of your weight of the evidence analysis?
A. I do look at -- I do categorize studies based upon my assessment of their reliability and their ability to be used to answer the question I'm asking, but I -- I already told you, I didn't do it the way it's set out here. I didn't have these specific five categories, no. That's not what I did.
Q. Okay. Other than the CIR 2013 publication, which you have said that you do not find reliable and you assign little weight to it, can you point me to another place in Exhibit 4 where you assign a specific category of weight that you have given to a particular study that you include in your weight of the evidence analysis?

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A. If what you're asking me is do I make a specific statement next to each study that I discuss about little weight or great weight, no, I don't do that, if that's what you're asking me.
Q. Okay. As part of the collection of documents that relate to Health Canada that was provided to us as part of your new reliance list, did you review a document entitled weight of the evidence -- or "Weight of evidence: General principles and current applications of Health Canada"?
A. Yes, I've seen that.
(Plunkett Exhibit 8 marked for identification.)
QUESTIONS BY MS. BRANSCOME:
Q. All right. We will mark this as Plunkett Deposition Exhibit Number 8.
All right. The document that I just handed you that's marked as Plunkett Deposition Exhibit Number 8, are you familiar with that document, Dr. Plunkett?
A. Yep, I've seen this before.
Q. Is this listed among the new materials that have been added to your

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reliance list?
A. I believe it was, yes.
Q. Okay. And so for this one I just want to direct your attention to the conclusion section -- well, let me ask you first: How does this document relate to the collection of documents with respect to Health Canada that you identified as relevant to your opinion?
A. It was one of the materials that they rely upon or they cite. That's the reason I pulled it. It was -- I pulled documents that they provided on the website that were cited.
Q. Okay. And if you could turn to page 11 of that document, there's a conclusion section. The first sentence of the third paragraph reads, "The given -- given the context-specific nature of each risk assessment and the diversity of tools and criteria applicable, transparent documentation of the specific application of the WOE approach is especially important."
Did I read that correctly?
A. Yes, you did.

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Q. And is your understanding of WOE that it is weight of evidence?
A. Yes, that's correct.
Q. Do you agree with this statement?
A. In a regulatory context, I do believe that that is true, because within the regulatory context when they do the risk assessment, there's a need to understand why decisions are made. So, absolutely, in a regulatory context, I would agree that this kind of transparency is even being adopted by EPA.
Q. And is it your opinion then that a different level of transparency is needed for expert testimony in court?
A. No, that's not what I'm saying. I'm saying that's a different process. And that's what part of this process is. It's understanding the ability to provide a dialog about what was done.
So as a result, this is something that is common to the work that I've done in the past. Even in a nonlitigation context with my regulatory

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clients, doing a risk assessment doesn't necessarily involve the same level of detail that a regulatory -- a regulator would apply to the transparency of the assessment. Not to say that it couldn't be done, but it's just -- I would say it's not necessarily typical.

Q. So this specifically refers to transparent documentation.

Do you see that?

A. Yes.

Q. Would you agree that the report that you have produced in the MDL does not have documentation of the specific application of the weight of evidence approach?

MS. PARFITT: Objection. Excuse me, objection. Form.

THE WITNESS: I disagree to an extent because I did attempt to provide in my report a description of the methods that I used and the resources that I've relied upon for a discussion of how those methods are used.

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And then in addition to that, I've attempted to lay out for you in my report a discussion of the pieces of evidence that I've relied upon, including some -- for some of those -- that's one of the reasons I got so detailed in the section on migration and providing you an analysis of each of the papers that I relied upon and what I thought was important within them that led to my -- the formation of my opinions.

So I disagree to some extent.

QUESTIONS BY MS. BRANSCOME:

Q. Okay. Turning back to what Taher did in classifying different studies into different categories of reliability. Have you done that type of analysis in the past where you have separated out different studies into different categories of weight or reliability as part of an overall analysis?

A. Well, I do that every time I do a weight of the evidence when I separate into categories first based upon the type of

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study. In other words, as I discussed many times in deposition, when you're talking about doing a human health risk assessment, there's certain types of data that are most relevant. I mean, when they use the word "reliable" -- I don't know that many of these studies have the same level of reliability as far as peer review, but they're -- for example, on the issue of migration, it's my opinion that the data from the human studies is a more reliable or relevant source of information. And I've laid out why, because of differences in the anatomy, things like that, with the data.

Q. Are you familiar with the term "binning exercise"?

A. Yes, I am. And that is certainly something that I have used in other aspects of work that I have done.

Q. Did you do a binning exercise in rendering your opinions and what you've provided to us in the context of your opinions in the MDL?

A. Yes, that's the exercise I start with. I'm binning them into human,

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animal, mechanistic, in vitro data. That's the first bins.

In fact, in the copper work we did, that's what we did. We separated the data into in vitro/only mechanistic information, animal studies, did we have human studies.

And we also looked at studies -- we had a separate bin of exposures like I do. I have studies that just address the issue of exposure potentially.

So, yes, it's -- it's consistent with doing that. It's -- essentially binning is just separating the information into groups based on what questions those -- those data can answer.

Q. Okay. Have you ever -- do you ever separate them into bins based on the level of weight that you would give a particular study?

A. I do that when I'm analyzing each of the studies within that group or that bin. That's what I do. I give them -- in my weight -- in my analysis, I weigh those studies based upon my judgment on the

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relevance, the reliability, the power of the study, the statistical analysis that's done, the inclusion in animal studies, in particular, of controls. Those are all parts of that analysis that I do. So, yes, I do do that.

And then in -- there have been exercises that I've done in the past with other individuals where we may have taken a yellow sticky note and put down on top of it animal data with exposure information, animal data without exposure information. That's the process that I'm doing when I am looking across the data. I'm separating those pieces of data into groups and what types of questions they can answer.

So that is consistent with what I do when I do a weight of analysis approach in the work that I do in both nonlitigation and litigation context.

Q. Okay. But we have no specific documentation of the different ratings that you gave the various pieces of evidence that you included in your weight of the evidence analysis, aside from occasional references to

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giving something less or more weight, correct?

A. Well, I certainly -- I told you I have not given numerical values that you're asking me, but I've attempted to do that when I have described them in groups, when I talk about human versus animal versus in vitro. Because I've already told you, I believe, it's my opinion that certain types of information are more informative than others. And so the more informative it is, the more weight you're giving it in -- obviously in your analysis.

But it is a different exercise than what is described here. And here I'm pointing to Exhibit 8. And it's a different exercise, obviously, than what a regulatory body is required to do where they are trying to come up with ways to increase the transparency when no one can go and actually talk to each of the regulators individually to understand what their thinking was.

Q. Okay. Returning to biological mechanism for a minute, why doesn't inflammation generally, including chronic

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inflammation, cause ovarian cancer?

A. Because it doesn't change the phenotype of the cell. It has to -- the -- and I discuss that. You have to -- you have to set up a chronic inflammatory process that leads to changes within the cellular phenotype to go from a cell that is -- that is -- is dividing normally to a cell that isn't.

So it's -- it's the same issue that you address even in a study in animals. Why do not all animals exposed to -- exposed to a chemical develop tumors. It's the idea that something has to be initiated beyond the exposure or maybe beyond inflammation to lead to the series of events.

And so, yes, it's recognized that you can get inflammation, and inflammation can go down the road in becoming a carcinogenic process, or inflammation can no longer -- can stay where it is. It doesn't progress beyond just a chronic inflammatory process.

Q. And so if you had a study that demonstrated that a particular agent causes

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inflammation, you would need more information in order to make the conclusion that that agent can in fact cause cancer, correct?

MR. MEADOWS: Objection.

THE WITNESS: You would look for more informative information, exactly, which is why, when I've talked about the individual constituents in the context of consistency on mechanism for cancer, I've pointed to documents where that information has been discussed.

So like when I talk about asbestos or cobalt or I point to the -- for example, the IARC assessment where they go through that -- that discussion of the fact that there's not just data showing that a biologically plausible mechanism may be inflammation, but there's also data to show that that can lead to tumor development as well.

QUESTIONS BY MS. BRANSCOME:

Q. Okay. How does talc change the phenotype of the ovarian cell?

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A. So this is one of the details we don't know, other than generally it's changing the phenotype to go from a normal cell to a tumor cell. That is being observed. When you find the presence of the tumor, that is what you're observing.

Q. Does pure talc with no other constituent components, can it change the phenotype of an ovarian cell?

MR. MEADOWS: Objection.

THE WITNESS: So that's a difficult question to answer with certainty because of the fact that I don't believe that we have assurance that any of the studies are done with essentially pure talc.

However, in the studies that claim to have been done with pure talc -- for example, the NTP study claims to have been done with pure talc. So if that is pure talc, truly is, then that study is an example of evidence for the chronic inflammatory process leading to preneoplastic lesions that are setting down the road

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mechanism towards cancer.

So there are data out there. The problem you have, I believe, in the literature is whether or not, based on the discussion that is becoming apparent now with sensitivity and ability to take the natural product and actually determine exactly what's in it, that I don't think there is the ability to assure that any -- any of these studies with the samples of talc they're using is absolutely, 100 percent, only platy talc. I think there's -- there's some concern about that. But certainly you will take -- you have to take what is discussed within the study as evidence from what they're claiming.

So many of the studies say we used asbestos-free talc or platy -- pure platy talc and we got a toxic response.

QUESTIONS BY MS. BRANSCOME:

Q. Would it be possible to design an experiment -- and now I'm talking about an

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in vitro or an animal experiment -- by which you would expose either cells or animal to talc with different constituent products to identify or separate out the individual effects of the components? Is that a study that you could design as a toxicologist?

A. I think that would be difficult to do, but I'm not saying impossible to do. And here's the -- there are some very specific considerations you'd have to put into that design.

I would argue that some of that is already available, where we have studies that have looked at the dose-response effects for toxicity with cobalt, with chromium, with asbestos.

When you get to asbestos and talc, it's more problematic because then the question is what is -- what is it? What are the specific characteristics in all the different studies of exactly what the asbestos was versus exactly what the talc was.

But I think you could attempt to do that, and then the question would be,

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being able to use that data not so much to -- not so much to identify a dose response for a certain insult, but to look at the fact -- look at potency differences across the compounds. And then there's the issue of then looking at additivity when you know you have a complex mixture.

So that could be done, but, again, it would be difficult to do based on what we know about talc, being able to really know that -- you would have to really be very careful that what it is that you're looking at is -- is not containing any of those things that we unfortunately know co-occur with constituents within the natural product.

But no one has done those studies. I point that out. I haven't seen that study that you're asking for. I have not seen somebody do that.

Q. And a study like that would be relevant in evaluating the potency of the individual constituents and what might actually be the driving factor for phenotypic change, correct?

A. Not necessarily. I would argue

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that we already have an answer to that by looking at the data that's been collected on the complex mixture itself. So the issue would be why -- the question is what do you gain by being able to say that we're only pointing to this constituent or that constituent. That isn't what is occurring.

What people are exposed to is the complex mixture, not just each one of those individual components. To me this is not a case of asbestos-only exposure. This is a case of exposure to consumer products that are talc that may have within them at any given time -- and data indicates that there are substantial chance that asbestos may be in -- is in certain of these products.

But my opinions are not dependent on there being asbestos there at a particular level or copper there -- or, I'm sorry, cobalt there at a particular level because my opinions are based on the observations we have on the complex product as it exists.

Q. And you recognize that different types of talc and different talc

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products have different constituent components in different amounts, correct?

A. Some can. I agree with that. That is true.

So if you're being broad, as in pharmaceutical-grade versus industrial-grade or chemical-grade, yeah, because they'll have a purity level assigned.

But as far as what the -- what the components are, it isn't always defined even specifically within that.

Q. Okay. And does the presence of oxidative stress in a tissue indicate that cancer will develop in that tissue?

A. Will definitively develop? Not -- I don't think you could say definitively develop, but it's certainly in the biologically plausible mechanism that's been understood to lead to chronic inflammation and also has been linked to cancer.

So that's the issue of not necessarily saying it has to be there, but it certainly is something that is observed routinely in cases where carcinogenesis has

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been linked to an inflammatory response. Oxidative stress is often a triggering mechanism.

Q. Does the body have protective mechanisms that limit tissue damage from oxidative stress?

A. Yes, which is why not everybody that's exposed to any particular chemical is going to get cancer. Some people will respond better. Some cells will respond better. Some individuals in a population at one time in their life may respond better.

Q. You would agree that in vitro studies do not account for the body's natural defenses outside of what exists at the cellular level, correct?

A. Depends on the in vitro study that's being done and whether or not there is components added.

So I've seen studies done where they take cells and then add extra levels of glutathione to try to protect the cells from certain stressors that could lead to damage, but I agree with you that an isolated cell on its own is a different microenvironment than

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an intact tissue, which is a different environment than an intact animal, which is even different than an intact human being. Yes, they're all -- you look at those levels of evidence or those types of evidence differently, depending upon the end points you're collecting.

Q. And so you would give lower weight to an in vitro study as compared to an in vivo study, for example?

A. Depends on the question you're asking. I would give a lot of weight if the question is what do I know -- if I want to try to understand the biologically plausible mechanism, some of those in vitro studies are some of the most important, because it's the only ones that allow us to answer a question.

If the question is higher level about what is the evidence to show that there's an increased risk overall for cancer or a hazard for cancer, then certainly you need to have more than an in vitro study.

So as -- so on -- if you want to layer it up, obviously, if all you had was in vitro data, you'd have much less

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confidence in the conclusions you can draw unless you had some in vivo data. In vivo data is going to allow you to interpret the in vitro data.

So certainly there would be more weight given in that assessment to the fact that you had in vivo data.

Q. And so when you made the statement that, for instance, you always give more weight to human data, is that true, or does that also depend?

A. Well, it depends on whether you have human data. So if I have human data and I have a doubt, any doubts at all, about whether or not the exposure-response relationship would be affected by the way the animal studies are designed, then, yes, I would give more weight to the human studies.

In a case, however, such as inhalation exposure assessments where there -- it's much better, actually, to do an animal study where we can do a dose response across different sizes of particles and actually observe lesions as they develop over time, which is why I love -- I love the NTP

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93 study of interim sacrifices, looking at that issue. That data is very reliable in order to understand the risk of lung damage as compared to a human study where we don't have those serial time points, doses that are defined tightly.

So -- and the relevance between those kinds of initial lung injury in certain animals versus humans match fairly well.

That's my problem, though, in the case with the perineal exposure. I'm saying to you, because of the route of contact -- we need to be able to get it there to the tissue -- the human data is extremely important.

Q. So is it fair to say that in some circumstances animal data gets more weight than human data and in other circumstances human data gets more weight than animal data? It is circumstance dependent?

A. I would put it a different way. I would say in some cases animal data is weighted in a similar manner to human data. I don't necessarily say it would get more

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weight, but it could if you only had one crappy human study, one really badly designed human study, and I had a GLP quality cancer bioassay then, absolutely. I mean, IARC does this. They look at that animal data and say, "This one tells us -- answers the questions we want to answer, and this very poorly designed case series isn't going to allow us to do that."

So you could, but I would say it's more the other issue, that you look at animal and human more on an equal basis if the relevance and the extrapolation can be done reliably.

And that's the question you have to ask, can I extrapolate from animals to humans in a reliable manner.

Q. Okay. Would you agree that the response to cosmetic talc can vary depending on tissue type in the body?

A. Yes, I would say that that is true, whether or not there's certain protective barriers in place, for example, yes.

Q. And so in order to draw

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conclusions based on a study of one cell type's reaction to cosmetic talc to another, you would need to understand the differences in similarities between those two cell types, correct?

MS. PARFITT: Objection.

THE WITNESS: It's a different question. So you were asking me about -- I didn't think you were just asking about cells. I thought you were asking me about like routes of exposure, dermal versus inhalation. Those things differ.

Cell types may or may not. That may or may not be true. Because if two cells -- two different cell types in the body share similar characteristics as far as the -- for example, if they're both epithelial cells or mesothelial cells, those type of cells you would expect to respond the same way.

But I would agree that, for example, a neuronal cell versus a GI cell versus a liver cell, there could

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be differences in how they would respond, yes, and so you would -- you would look at those things individually.
QUESTIONS BY MS. BRANSCOME:
Q. And so it's important to understand the differences and the similarities between the different cell types before drawing conclusions using studies from different cell types?
MS. PARFITT: Objection.
MR. MEADOWS: Objection.
THE WITNESS: I certainly think you should consider the cell types that are being used and whether or not those cell types are ones that are relevant to your risk assessment question you're asking, yes.
QUESTIONS BY MS. BRANSCOME:
Q. Okay. You would agree as a toxicologist, dose is an important part of a toxicological analysis of an agent, correct?
A. If you're doing risk, yes. If you're only doing hazard, it may not be as important. It depends upon the question

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you're asking about hazard.
Do you want me to explain?
Q. I do want you to explain the difference between a risk analysis and a hazard analysis.
A. Okay. So in an initial hazard analysis, if the question is, is there a hazard associated with exposure, let's say, by inhalation, it may not matter whether it was a high dose or a low dose study. Both of those can identify hazard.
Then you ask the question: Is there a dose-response relationship? That's the next step beyond hazard.
So hazard is -- to me is identifying the end points that you're going to monitor for toxicity, sort of the target organs, those things, and so whether or not there's a dose-response study available, it wouldn't be as important.
But certainly when you go to that next step to assess risk, you'd like to be able to see whether or not there is a dose-response relationship in the effect that you're assessing.

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Q. Okay. And in your -- in your report, as part of your risk assessment that you did in the MDL -- this is paragraph 12 on page 8.
A. Yes, I'm there.
Q. Okay. You state about two-thirds of the way down the paragraph that "weight of the evidence methods were critical to defining the literature that identified the hazards of talc exposure as well as defining the dose-response relationship between talc exposure and the risk of adverse health effects."
Did I read that correctly?
A. You did. That's correct.
Q. All right. Is it your view that in the case you have reached an opinion that defines the dose-response relationship between talc exposure and the risk of ovarian cancer?
A. It depends what you mean by define. I can tell you what I mean in this sentence, and maybe that would help you.
Q. Dr. Plunkett, it is your report. And so I am asking you, using your

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own definition of "define," have you rendered an opinion that defines the dose-response relationship between talc exposure and the risk of ovarian cancer?
A. I have formed opinions about the dose-response relationship generally, but unfortunately -- I answered that question for you earlier when you asked me, I think, about is there -- I don't know if you used the word "threshold," but I did.
So the available information doesn't allow us to identify an ultimate threshold, for example, in the case of women exposed to talc perineally and their -- and their development of ovarian cancer.
Instead, in defining the dose response, what we can do with the data -- and that is what I attempted to do. This is where you look at defining the dose response in the animal studies, which we can look at, or defining dose response in cell studies, showing that as the dose increases, the hazard and the risk increase. So risk actually you quantify. There's a certain response at this dose and a different

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response at the next dose, or have we plateaued, that the responses are the same as dose increases.

So that, I did do that as part of my assessment, trying to define the dose as far as how that linked to the responses in each of the studies I looked at.

Q. You would agree, though, that some studies did not show a dose relationship between talc and ovarian cancer or the clinical signs that were indicative of the potential for development into ovarian cancer, correct?

MS. PARFITT: Objection.

THE WITNESS: If you're talking about the human data; is that what you're referring to? Or are you talking about all -- any of the data?

QUESTIONS BY MS. BRANSCOME:

Q. Any of the data.

A. So I would disagree on the animal data. I think on the animal data they often -- most of the animal studies I've relied upon have looked at more than one dose or at least looked a no exposure versus a

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dose, and most of them have looked at more than one dose.

In the case of the human studies, unfortunately, some of those studies were not designed to be able to define dose. In other words, the questions weren't asked, for example, of the individuals even in the prospective studies. Some of those included -- did not include the information collected on frequency and duration of use.

So if it's not collected, obviously, I don't have it to look at. And that's one of the limitations of human epidemiological investigations, is that it often is not designed appropriately to look at dose response.

Q. Is it your opinion that there are no studies looking at talc and the risk of ovarian cancer in which the authors of the study have concluded there was no clear pattern of increased risk with dose?

MS. PARFITT: Objection.

THE WITNESS: No, that's not what I've said. No. It's very possible that an individual paper

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or -- that they may make a -- an author may make a statement, but I'm talking about looking -- this is weight of the evidence. I'm looking across. And I'm saying, across the data, when I look at the human data versus the animal data, for example, versus in vitro studies, the in vitro studies and the animal studies allow you to look at dose response for talc toxicity.

The -- even the animal studies allow you to look at dose response for development of precancerous lesions, you're on the way to cancer, for example, in the NTP studies.

And then in the human studies, some of those studies are designed such that the authors could draw conclusions about dose response and some are not.

Even in some of the studies where they attempted to look at dose response, some of the authors indicate they don't see an effect. So that is

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true. And part of that may be driven by the design of the study, the number of individuals in the study, the way that the questions were asked. There's limitations on the way that information is collected.

If you want to look at each study, we can, but --

QUESTIONS BY MS. BRANSCOME:

Q. So my question to you, whether you agree or disagree with the author's conclusion, is simply that if you look at the overall animal and human studies that you cite in your report or have considered on your reliance list that look at a potential dose-response relationship for talc toxicity, do some of those studies conclude that there is not a dose-response relationship?

MS. PARFITT: Objection.

THE WITNESS: I disagree for talc toxicity, but I would say if you're going to limit it to the issue of the ovarian cancer response, I would agree. I have seen that in some of the studies.

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I think talc toxicity, I don't know if anybody has made the comment -- I would doubt it -- that there is no dose response for toxic effects of talc.
QUESTIONS BY MS. BRANSCOME:
Q. Okay. You discuss in your report -- wait a moment. It's in paragraph 58 on page 38. And I just want to make sure I understood what you were citing here.
In paragraph 58 you state that "It is important to remember that administration of even a single dose of talc in animals has been shown to produce adverse effects locally at the site of the exposure."
What are you referring to there?
A. Acute doses. In other words, in studies that have described installation of a single dose of talc in some form into a tissue, that they are observing adverse responses.
An example of that may be the -- I think it's Hamilton. Is that the

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one where they stilled it into the ovaries with a single dose?
Q. So these are large-dose exposures?
A. Well, not all --
Q. Or are they, I should say?
A. I don't know that they all are, no. There are -- there are -- I don't think I have attempted to quantify large in this sentence.
What I'm stating here is not an issue of large versus small. It's an issue of the fact that there are toxic effects with single exposures. And I'm just making the comment -- this has to do with hazard, right? It's the idea even a single dose -- or a single exposure you can get irritant, inflammatory reactions at the site of exposure. And that's all I'm trying to say. That's why I'm citing as reviewed by EPA. I believe EPA even makes a very similar statement.
Q. Okay. Do you take into account -- there are some studies for which -- at least my reading of your report

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is that you give them less weight because you believe that the individuals who conducted the study had been paid by either a company or agencies that had some investment in the outcome of the study; is that correct?
A. Is that my opinion?
Q. Yes.
A. For any particular study, you'll need to show me what you're pointing to. I do have opinions about some of the work by Drs. Huncharek and Muscat, yes. I think I address that specifically, and that has -- that's not so much to do with my weight of the evidence; that has more to do with transparency and what was being disseminated to the public and disseminated to the FDA as far as evaluations.
That's a different issue than the weight of -- the weight of -- the weight of the evidence assessment for risk. I think those were separate.
Q. So then I'll ask you that.
In doing your weight of the evidence analysis for risk, have you discounted the weight that you've given to

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any particular piece of scientific evidence based off of potential affiliations of the authors?
A. I certainly did with the CIR review document. I've already told you that. And that's because I have evidence that shows it's not just an affiliation issue, but it's actually -- it's more -- it's more important than that.
Q. Are there any other examples?
A. I think that's the only one right now as I sit here that I can tell you that I had identified as carrying little weight because of an issue of either authorship or input in the way it was described.
There are certainly studies within my weight of the evidence evaluation, some of which were performed by industry. I certainly look at that issue, but unless I have -- have a reason to believe that there's an inherent bias based on something I know, they go into the weight of the evidence without making a correction for that.
In many cases that I work in

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litigation, I will find situations like the situation here with Huncharek and Muscat where I have, for example -- I think this came up in the Risperdal litigation for me. It's the idea that there was a series of papers put out by an individual investigator where documents that I could get access to show me that indeed their analysis was not done by them but it was ghostwritten by somebody else. So that gives me pause, although I would never have known that unless I had access to internal documents.

So initial weight of the evidence I did not discount it, but then I went back and had to reevaluate the role those studies played in my overall assessment.

Q. Do you take into account in any way in evaluating the weight of a study if it is conducted by someone who serves as an expert on behalf of the plaintiffs in the active litigation?

A. It would be the same -- same issue. I certainly consider it as part of what I look at, but just like if they were an

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expert for the defense versus an expert for the plaintiff, you judge that information based on what you know. And if I don't have information to discount it, I will not discount it.

But absolutely, I understand. Just as people we all -- look at some of the things I've published where I have said my work was sponsored by the American Chemistry Council. You know, people -- that's why you disclose the conflicts. You put it there so people can weigh it if they want, but it doesn't mean you discount the work automatically.

And so I think for any paper, plaintiff, defense, whoever it is that's writing it, you need to consider it based on the information you have. And if you believe that you have information to indicate that there's some issue with the reliability of the analysis, then absolutely you consider that.

Q. So, for example, when you rely on Dr. Longo's characterization of the constituent components in samples that he has

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tested, that he reports are Johnson's baby powder, did you also consider the work that was done by experts that have been retained on behalf of the defendants to characterize the components of Johnson's baby powder? Do you give them equal weight?

A. So I haven't seen a variety of the documents that you're talking about, so -- because I have not worked in the litigation cases that have involved asbestos only. So -- which I think is where those documents are.

In the litigation I -- in the litigation I worked in, I am aware of what other experts on both sides have said. I don't believe I've seen an analysis from a defense expert that is -- that is like Dr. Longo's, at least in the litigation I've worked in. Certainly I would consider that and look at that if it's available, and I would consider it.

I would point out, Dr. Longo's analysis is not the piece of evidence that you start with, though. You start with what I discuss in the published literature first,

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because there are published documents out there in the literature that describe exactly what Dr. Longo is now describing.

Q. What published documents are those?

A. Those are Dr. Blount's reports in 1991, which is before the litigation came about, is my understanding.

There's also -- there's five or six. I can tell you the paragraph.

Q. For Johnson's baby powder, I would be interested in that, yes.

A. So I -- I'll have to look and see if it's Johnson's baby powder only, but certainly there is other evidence on the issue of asbestos contamination and specifically in talc.

So I -- you want me to find the paragraph for you?

Q. Please. If you think there is published literature documenting asbestos in Johnson's baby powder, I would like to see that.

A. So this is my paragraph 32. And I'd have to pull each of these articles

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out because I don't recall what each of them says. But I'm pointing to Paoletti, Blount, Mattenklott, Moon, Gordon, Anderson, Rohl, Pooley and Rowlands, Blejer and Arlon, Cralley, Millman.

And then I cite -- and then of course the next piece of evidence is there are actually documents from J&J and Imerys that show detection of asbestos or asbestos-like minerals in talc.

Q. As you sit here today, can you identify which of these published articles that you list in paragraph 32 relate to Johnson's baby powder?

A. I would have to pull them to answer that.

Q. Okay.

A. As I sit here, I'd have to pull them. But I would refer you -- I know at least some of them do based on the statement I've made, but...

Q. So you did not make an attempt in this paper to identify which products were being analyzed in these specific articles. It's not indicated on the face of this

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paragraph, correct?

A. I don't tell you on the face, but you if read the sentence I said, "When commercially available, talcum powder products were analyzed, including powders sold by Johnson & Johnson. The data has shown that the powders contained varied levels" -- and I'm saying "fibers," so it's just asbestos -- "including fibers that stated to be asbestos."

So to tell you which of those, I'd have to pull them. And I apologize, I didn't bring them all with me.

Q. Have you been provided -- you're aware that Dr. Blount's paper does not identify Johnson's baby powder in the face of the article, correct?

A. I believe that's true. You'd have to go to her deposition, I believe, where she's given -- where she discusses what the source of that was, and maybe even a -- there may even be a separate document, actually, not a deposition, that was -- that was in the files of Johnson & Johnson that goes along with that, but I'd have to go

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look.

Q. Have you reviewed Dr. Blount's deposition?

A. I have reviewed a -- something by Dr. Blount. Whether it was trial testimony or deposition, I have seen something, yes, that she has said regarding this issue.

Q. To the extent that there is confusion about whether or not a sample tested by Dr. Blount is in fact Johnson's baby powder, would you reduce the weight that you give that particular piece of evidence in evaluating whether asbestos has been present in Johnson's baby powder?

MS. PARFITT: Objection. Form.

MR. MEADOWS: Objection.

THE WITNESS: I don't know reduce the weight because -- because there's -- there are plenty of documents here that talk about that.

I would consider it -- certainly it would -- it's not so much weight. It's a different bin. We'll call it a bin, a different bin of

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information. There's information on talc powders generally, and then there's some information that's specific to certain body powders.

So certainly -- would I pay attention if they identified it? Yes.

But in the statement I'm making here, I'm not claiming that every one of these is relating to just the powder sold by Johnson & Johnson. This is across the available information that's public and then also the information that's available in the files of Johnson & Johnson.

QUESTIONS BY MS. BRANSCOME:

Q. What is your definition of asbestos?

A. My definition of asbestos is exactly what the different documents describe it typically. It's a fibrous mineral, typically. It occurs in a variety of different forms. Most of the times they'll say "asbestos." Sometimes they'll say "chrysotile." Sometimes they'll say "tremolite." Sometimes they'll say

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"anthophyllite." Those are the three most common ones I see. But those are all mineral forms of asbestos.

So just like IARC puts those all within one bin, I'm putting those all in one bin because they have a similar toxicity profile.

Q. Is it your view that each of the different types of asbestos has the same toxicity profile?

A. They all have the same ability to cause cancer, but they have different potencies. So they do have -- there will be some differences in the dose response and the potency of them, but certainly they've all been linked as being carcinogens by IARC.

And I would agree, when you look at their data, there is data and evidence to indicate that.

Q. Which type of asbestos is the most potent?

A. For which end point? For lung cancer? I believe chrysotile is. For other end points, I'd have to go look. I mean, chrysotile is the sharp -- is the sharp --

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the sharded-type structure.

But there's data on fibrous -- the fiber -- the fibrous forms of asbestos rather than the -- or the amphibole forms of asbestos as opposed to chrysotile, which is the serpentine form.

Q. Do you consider yourself an expert in asbestos?

A. Not in --

MS. PARFITT: Objection.

THE WITNESS: Not the geology of asbestos, no.

I have expertise in toxicology as it relates to interpretation of the data related to asbestos. I have never give -- given testimony in a case on asbestos, but it's something I've studied in the past in my work as a toxicologist, not as a testifying expert.

QUESTIONS BY MS. BRANSCOME:

Q. What role does your analysis of the possibility that there may be asbestos in Johnson's talcum powder products play in your risk assessment in the MDL?

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A. Has to do with the fact that we have a complex mixture that has multiple carcinogenic substances.

And asbestos is important from the aspect of the way that it has been assessed even by regulatory bodies, the idea that even very low levels of fibers pose a cancer hazard and a cancer risk in individuals have been shown to be carcinogenic.

So that's what I'm saying about potency of asbestos is different than potency of some other carcinogens that you might look at. But the importance of it is it's a complex mixture, talc, body powders, a complex mixture that includes constituents that are known human carcinogens as well as some that are -- been ranked other ways by regulatory bodies.

Q. If Johnson's talcum powder products do not contain asbestos, does that change your opinion with respect to the risk they pose with respect to ovarian cancer?

A. No, and I think that was very clear if you looked at my first report. So

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even -- there's -- I don't think in any of my reports I've opined that without looking at the complex mixture that we wouldn't be here.

In other words, I have not opined that if it doesn't have -- if it doesn't have asbestos, it's not a risk. I have not opined that, and I don't believe that, because I think there is independent risk for the fact that we have a complex mixture of talc that has been tested and shown to be carcinogenic.

It's my opinion, I told you -- maybe it wasn't you. I may have told this yesterday, I'm sorry, to Mr. Smith that I believe that there is evidence to show that there is a significant exposure to asbestos based on the data that's been collected.

But certainly, you know, in some -- the data has shown that in the assays that have been done or the analyses that have been done that you can't say that talc is asbestos-free.

Q. Well, so --

A. So --

Q. -- the question I have

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specifically relates to ovarian cancer.
Is it your view that through an exposure route that is relevant for ovarian cancer, that the use of Johnson's talcum products involve a substantial exposure to asbestos?
A. I believe based on the use of the products that -- where the data has been collected that there would be a substantial exposure to asbestos, regardless of how you're exposed, perineal -- perineally or by inhalation.
Q. What is your basis for reaching that conclusion?
A. It's looking at the number of fibers that have been detected in the products, in looking at the -- the widespread nature of the presence of asbestos fiber -- asbestos in the talcum powder products and the fact that even though it's at a very low level by their -- their level of detection, again, can't be said to be asbestos-free.
So regardless of whether it's talc that's being applied perineally or a talc that you're inhaling while you're

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applying it perineally, the fibers are still going to be present within that talc.
Q. Have you or anyone done an analysis of the dose of asbestos to which someone might be exposed perineally?
A. I haven't done a specific calculation, no.
Q. Has anyone done that calculation?
MS. PARFITT: Objection. Form.
QUESTIONS BY MS. BRANSCOME:
Q. That you have seen?
MS. PARFITT: Objection.
THE WITNESS: I'm trying to remember whether I saw that done in any of the documents related to Dr. Longo.
I don't know. I'd have to go look.
QUESTIONS BY MS. BRANSCOME:
Q. Okay. So as you sit here today, can you give an opinion to a scientific degree of certainty, reasonable degree of scientific certainty, that an individual would be exposed to a dose of

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asbestos above background through the perineal use of Johnson's talcum powder products?
MR. MEADOWS: Objection.
MS. PARFITT: Objection.
THE WITNESS: I don't think that's the opinion I have formed to date, but certainly the opinion I have formed is that the data I have seen indicates that you can't separate out talc without asbestos versus talc with asbestos in the information that's been collected. Because there's -- all -- the information that's been collected has shown there's no evidence that asbestos-free talc is available.
If by asking that question you're trying to say that it's the asbestos alone that's causing the cancer, that is not my opinion. So that is when the dose issue would become very important for asbestos.
QUESTIONS BY MS. BRANSCOME:
Q. Okay.

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A. So that's -- so that's a different question I have not answered.
Q. And in reaching your opinion that there is no evidence that asbestos-free talc exists, you have not been provided with the reports by the defense experts, including Dr. Matthew Sanchez, analyzing Johnson's talcum powder products for the presence or absence of asbestos, correct?
MS. PARFITT: Objection. Form.
I think you're aware that the MDL expert reports have not yet been provided to us.
MS. BRANSCOME: Yeah.
MS. PARFITT: I'm just making a point.
THE WITNESS: I have not seen a report by Dr. Sanchez. I assume I will, because typically after -- later in the litigation, once all experts have been deposed or revealed, I'm usually given defense expert reports and their deposition testimony. So I expect to see that; I just haven't seen it yet.

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QUESTIONS BY MS. BRANSCOME:
Q. And you haven't seen it in any of the cases in which you've rendered an opinion, correct, not just the MDL?
A. Well, none of the cases that I have worked in have involved the issue of looking for asbestos exposure.
The cases I have worked on have been talking about talc exposure that may include asbestos as a constituent, but it wasn't focused on asbestos exposure.
So, no, none of the cases I worked on have provided testimony in that area.
You understand what I'm saying?
Q. Let me just make it clear. You have not, in any of the cases in which you have offered opinions with respect to the contents of talc, been provided with an expert report or testimony by Dr. Sanchez about what he did or did not find in Johnson's talcum powder products with respect to asbestos?
MS. PARFITT: Objection. Form.
THE WITNESS: So I can't tell

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you that I have not. I don't recall it. That's all I can say. I don't recall that name.
QUESTIONS BY MS. BRANSCOME:
Q. It's certainly not something you discuss in your report, correct?
A. No, I do not. And I don't know that it's in my reliance materials. That's why I'd ask you to look there, because if it's in my reliance materials, then I've seen it.
Q. Okay.
A. And I mean big reliance material list, not my reference list.
Q. All right. With respect to the other potential constituents of talc, have you done any analysis to provide an answer as to how much -- what dose of chromium, for example, an individual might be exposed to through the perineal use of Johnson's talcum powder products over a lifetime?
A. No, and I have -- well, I know it's a separate deposition. We discussed this yesterday. No, I have not done a -- a calculation of a potential dose with perineal

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application for any of the heavy metals. So the three that I've mentioned, no, I have not done that calculation.
Q. You would agree, based on your training and experience as a toxicologist, that in order for an agent -- and we can talk specifically about a metal -- to present a risk of cancer it needs to be bioaccessible, correct?
A. If by bioaccessible you are not limiting that definition to solubilized into the blood and carried systematically, yes, I would agree with that. Bioaccessible meaning it has to be in a form that can somehow interact with the tissue, yes, I agree with that. But it could be as simple as tissue contact versus needing to be solubilized.
Q. Okay. Is silica bioaccessible?
A. It depends on the form of the silica. So silica particles can be bioaccessible if inhaled and found on the surface of the lung. That can cause injury at the site of the lung. So that's an accessibility to that particular tissue that it contacts.

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Q. We talked earlier -- it's somewhat related to bioaccessibility, but we talked about the way in which different particles might move specifically through the genital tract in women.
Do you recall that?
A. Yes. A general discussion.
Q. Yes.
And when you testified that starch and talc might not move at the same rate, do you have an opinion as to which might move more quickly through the tract?
A. I haven't formed that opinion, no.
Q. Okay. And do both talc and starch particles remain in the body for the same length of time?
A. I haven't done an analysis to see if the data tells us what the -- what the differences might be. I would expect there to be differences, which is what I told you earlier, because I would expect the starch to be able to be solubilized, where I would not necessarily expect the talc to act in that same manner.

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Q. Is cornstarch capable of causing an inflammatory process?
A. It can. It is -- but it is -- it's a different level of risk for inflammatory responses than is talc, just by its chemical nature.
Q. Have you done an analysis in your report that examines the differences between the inflammatory response that can be triggered by talc as opposed to cornstarch?
A. I haven't analyzed inflammatory response. Instead, what I've done is done a comparison of what the toxicity -- the differences in the toxicity potential have been described in medical literature, and I cite -- I have a paragraph where I cite to some sources that talk about the differences in the toxicity potential or biocompatibility of starch versus talc.
Q. Now, I had a question about your supplemental report that was marked as Exhibit 3 to the deposition.
At paragraph 67...
A. Okay.
Q. You identify here six heavy

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metals - arsenic, chromium, lead, cobalt, cadmium and nickel - that in your supplemental report dated August 29, 2018, you say have been reported across lots of talc powders.
Do you see that?
A. Are you in -- now you're in my MDL report or here?
Q. No.
A. Oh, so where are you? I'm sorry.
Q. Same report. It's the sentence that begins at the bottom of page 6.
A. Okay. Hold on.
About that they have varied at the levels --
Q. Yes. So you identify six different types of heavy metals.
Do you see that there?
A. Yes, I do.
Q. Okay. And the question I had for you was that in your report in the MDL, if you look at paragraph 36 --
A. Yes.
Q. -- you identify -- you identify

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only three heavy metals: chromium, cobalt and nickel.
Do you see that?
A. Yes.
Q. Why did you remove three of the heavy metals?
A. It's not so much removing. Those three heavy metals that I focused on in my MDL report are ones that have been talked about with a similar mechanism of action as far as irritation and biologic -- biologic plausibility mechanism being irritation and inflammation.
So that's why I focus on those three, which may not -- which is not necessarily the case for some of the others, even though they're also -- have a carcinogenic hazard, pose a risk.
Q. So in your -- as part of your risk assessment that you performed in the MDL, are you offering the opinion that to the extent they exist in any of the Johnson talcum powder products, that arsenic, lead --
A. Cadmium.
Q. -- and cadmium play any role in

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the risk of developing ovarian cancer?
A. That is not an opinion that I would be offering in the MDL.
Q. Okay. Now, you talk about these heavy metals having been classified by different agencies as either known probable or possible human carcinogens, correct?
A. You're in my MDL report again?
Q. Oh, yes.
A. Okay. I'm sorry. Okay. Let me get there.
Yeah, I do have that discussion. I'm just trying to find it.
Q. Sure.
A. Okay. Yes, I'm there.
Q. Is it your view, based on your expertise, that because a compound can cause one type of cancer, it can cause all types of cancer?
A. No, not necessarily. It depends on the -- well, it depends on a couple of things. It depends on what's been studied. Have all types of cancer even been studied. And then it also -- it also depends upon, I believe, the route of exposure as

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well. So can it get to where it could cause that, could it distribute there. And then in addition to that, what data has been collected. Is there enough data, for example, to show that there's extrapolation from animals to humans in the types of tumors or is it -- or if we have good human data, then we would focus on the types of cancers that you're seeing in humans, for example.

Q. Okay. But you recognize even where there is complete data some compounds can cause one type of cancer and they are incapable of causing another type, correct?

MS. PARFITT: Objection. Form.

THE WITNESS: I don't know about incapable, but I would agree that you certainly would see -- you could potentially see different observations.

If you're talking about animals versus humans, or are you talking about --

QUESTIONS BY MS. BRANSCOME:

Q. If humans.

A. Based on what you had seen in

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the animals; is that what you're asking me?

Q. Yes.

A. Yes. So, yes, there is not always a one-to-one concordance. So that's why -- that's why I made the comment that it's important to have some human data or experience, so that you can put in context the data you collected in animals.

I would say to you there are certain kinds of tumors in animals, for example, that are shown to be not relevant at all to human risk assessment. Like four stomach tumors in rats is an example. I've dealt with that one a lot.

Q. What types of cancer -- type or types of cancer are the basis for the classification of chromium as a known human carcinogen by IARC?

A. So I have to pull it out, but I believe that there may be some GI cancers and maybe some skin cancers, but I'm not sure. I've got it pull it out. It's been a while since I've looked at it.

Q. Okay. Have you done an analysis to evaluate whether or not the types

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you can extrapolate with scientific basis from one type of cancer cause to ovarian cancer with respect to the heavy metals specifically?

A. Well, I haven't attempted to that, because I haven't attempted to define a independent risk for each of those metals individually.

The issue -- the issue I have with those metals is -- there's a paragraph here where I talk about pathogenesis of carcinogenesis, where I talk about different stages of cancer development and the fact that inflammatory responses may be operating at all those different stages.

So the issue is you have potential -- you have compounds that are known to produce cancer or have been shown to have a potential risk of cancer. They share a similar mechanism to talc, so as a result of that, they factor into your risk assessment as far as there being an exposure to a mixture.

But on the issue of ovarian cancer, I'm looking at the data that's been

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collected on talc itself, which would be talc with the constituents that could include the metals. But certainly I'm not saying that it is -- without the presence of one or the other of these there would be no risk of ovarian cancer. I'm not saying that either.

Q. So my question is, though, can you point me either to scientific literature directly documenting that these heavy metals can cause ovarian cancer or to scientific literature that enables you to extrapolate from the types of cancer that they are known or believed to cause to ovarian cancer?

A. So I -- on the issue of can I point you to the data on ovarian cancer, I'd have to go back. I can't answer that without looking at the assessments.

But on the other -- second question you asked me, that's the question I was just trying to answer before. It's the idea that regardless of where the cancer is developing, the fact that these compounds have the ability to stimulate similar toxic responses in tissues could lead to a -- setting up a situation where the -- where the

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tissue is primed for cancer development.
Q. And do you have --
A. And so that --
Q. Sorry.
A. And that has to do with the basic science of carcinogenesis when you look at underlying mechanisms, especially with tissue contact, direct tissue contact, with irritants or inflammatory processes.
But I would -- I am not -- I have not formed the opinion, again, that with or without either one of these that I would expect ovarian cancer to be the target. I'm saying that ovarian cancer risk is increased based on exposure to talc, which includes a variety of constituents.
Q. Okay. And do you cite anywhere in your report to studies documenting -- I know you said you'd need to go look at them, but I'm asking if it's in your report anywhere a discussion of any studies showing that the particular heavy metals that you cite as potential constituents of Johnson & Johnson's products have been demonstrated to increase a risk for ovarian cancer on their

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own?
A. So, no, I haven't addressed that in my report. And again, I think that's inconsistent with the way I'm using these data. But that's fine. I mean, no, I haven't done a specific assessment of ovarian cancer risk with each of those metals individually.
Q. I would ask the same questions for the different fragrance constituents that you allege in your report are potential carcinogens.
Have you done any analysis, and can you point me to any scientific studies that establish that those particular compounds are capable of causing ovarian cancer?
A. No, I haven't done that analysis, but, again, general principles of toxicology and cancer risk assessment, when you look at the presence of multiple -- excuse me, multiple carcinogens with similar mechanisms of action, you would assume in your risk assessment that those risks could be additive.

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So, again, that's what I'm pointing to and why I have cited the data.
Q. Now, you talked about -- when we were discussing mechanism, you said that inflammation alone is not necessarily sufficient to cause cancer, correct?
A. Yes, I did.
Q. All right. Do you have scientific studies that show that any of the heavy metals or the fragrance constituents that you identify as potential carcinogens create -- generate phenotypic changes like you discussed were next for the formation of cancer?
A. I believe that data is available on nickel. I need to go back and look at chromium and cobalt, but I do believe with nickel you'll find similar data on tissue irritation and inflammatory processes.
Nickel is also a sensitizer, so it has interaction with the immune system, so I do believe that for nickel you can find some of that data.
Q. Okay. But as you sit here today, can you point me into any of that

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that's discussed in your report?
A. No specific discussion other than, again, all -- the IARC -- I'm citing to the IARC assessments, and the IARC assessments for each of those discuss carcinogenesis and a biologically plausible mechanism being linked to the ability of these compounds to induce oxidative stress and/or inflammatory processes.
Q. Okay. In your opinion, you talk about the mixture of constituents that are involved in talc.
Have you done any analysis to look at how the different constituents interact with each other?
A. Well, yes, that's my issue at looking at underlying mechanism.
But are you asking me -- I certainly don't have a -- the only studies that I have to rely upon on the interaction of the mixture is the actual studies on the powders themselves, where we know that the powders contain constituents other than just platy talc.
Q. Okay. And do the constituents

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need to have the same underlying potential carcinogenic mechanism for them to have an additive effect?

A. By general principles of toxicology, yes, you look at mode -- mode of action or mechanism of action before you apply that additivity principle to the cancer risk assessment.

Q. And so as you sit here, you believe there have been scientific documentation that nickel might operate through the same biological mechanism as you purport talc to operate, but you're not sure about the other heavy metals or the fragrance constituents; is that correct?

MS. PARFITT: Objection.

THE WITNESS: For the fragrance constituents, I'd definitely have to pull because I haven't looked at that individual assessment in a while.

For these three, what I do know is that they do share the ability to at least induce oxidative stress.

What I can't recall for chromium and for cobalt is whether

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they're taking it the next step from oxidative stress to inflammatory process. I believe that they do, but I'd have to check, whereas I know nickel has been shown to lead to an inflammatory process after oxidative stress has been induced.

QUESTIONS BY MS. BRANSCOME:

Q. And you would agree, even more than requiring an inflammatory process, you would actually have to see that these compounds can generate phenotypic changes, correct?

MS. PARFITT: Objection.

THE WITNESS: Well, we know they do because they've been shown to be carcinogenic. If you've been shown to be carcinogenic, you've done a phenotypic change in the cell from a normal cell to a cancer cell.

So we know they have the capability to induce tumors, or cancer, all three of those, at least in animals if not in humans as well, because two of them are known human.

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So those two -- we'd have human data to show that.

But on the issue of cobalt, it may only be -- I need to go back and look, but it may indeed just be animal data.

QUESTIONS BY MS. BRANSCOME:

Q. And so your basis for that would be the IARC classification?

Is that where I would go to look if I wanted to look at it after this deposition?

A. I'd go to the IARC reviews. I'd go to those three which I believe I have cited down here for you and given you where to go to find them.

Q. Okay. You discuss in your report -- and if you'd like to reference it, it's paragraph 69 on page 47 -- the concept of genotoxic and nongenotoxic carcinogens.

Do you recall that?

A. Yes.

Q. And as you sit here today, is it your opinion that talc is more likely a nongenotoxic carcinogen?

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A. As the direct insult, yes. And I would like to -- I would like to point out that in the literature -- the reason I have this paragraph here is because in the literature in the past, in the area of chemicals, it's been -- toxicologists have attempted to put two bins, direct genotoxic insult versus nondirect genotoxic. It doesn't mean you can't get a genotoxic event after the initiation.

So I want to make sure you understand that. I'm not saying that there is no possibility of this chemical in its -- in its process of inducing cancer leading to indirect genotoxicity, but I'm talking about the direct mechanism at the site of the cell.

So talc, for example, has been shown to not be genotoxic in cells. And so that's why I believe, then, when I look at the rest of the data that fits, that it fits the definition of a nongenotoxic carcinogen by its initial mechanisms to induce cancer.

Q. Okay. And if talc is, in fact, a nongenotoxic carcinogen, it would suggest that there is likely a threshold dose below

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which it does not have a carcinogenic effect, correct?
MS. PARFITT: Objection.
THE WITNESS: It is possible, and that's the problem. In order to fully assess that, you would have to have the data to prove it.
But that's the assumption. You assume with nongenotoxic carcinogens that you could identify a level where you wouldn't turn on that indirect mechanism. So that -- yes, that is true.
QUESTIONS BY MS. BRANSCOME:
Q. And you have not been able to identify, nor can you point to, scientific literature that identifies a threshold -- a threshold dose for talc with respect to its carcinogenic potential for ovarian cancer, correct?
A. Not a specific dose, but I think that's why I mentioned to you -- and I -- I think that's why Canada, when you look at their document, they talk about discouraging routine use generally. So it's

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the issue of what -- single use of a body powder or an occasional use is a different risk assessment than routine use.
So if you want to talk about thresholds that way, that's very imprecise, but you could do that. You can talk about whether or not there -- I do believe there's a different risk profile for one or two uses of talc body powder versus a risk profile of somebody who uses it routinely, because I think that fits that threshold definition. It's the idea that you have limited availability for enough particles to migrate to lead to the tissue toxicity that it cannot be recovered from or repair.
Q. You're familiar with the concept of the precautionary principle, correct?
A. Yes.
Q. All right. And you understand that Health Canada may have made recommendations with respect to product usage that are purely precautionary, correct?
MS. PARFITT: Objection. Form.
THE WITNESS: I disagree that's

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what they've done, but is it possible that they would do it? Any regulatory agency, it's possible they could do it, yes.
QUESTIONS BY MS. BRANSCOME:
Q. Do you have any information with respect to Health Canada's decision-making, other than what you have read on the face of the documents?
A. That is all I have to look at is what is provided on the website.
Q. Okay. And so the statement that you think Health Canada was suggesting a dose threshold by their statement of discouraging routine use, you're basing that entirely on what you read on the piece of paper, correct?
MS. PARFITT: Objection. Form.
THE WITNESS: Well, that's what they state. So, yes, I'm -- I am telling you what I see on their website. If that's what you're asking me, yes, that is true.
QUESTIONS BY MS. BRANSCOME:
Q. Okay. Can you point me --

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well, do you discuss -- have you looked at, as part of your opinion specifically in the MDL, the studies exploring a potential link between asbestos and ovarian cancer? Just asbestos.
A. Some of the studies, yes, but I have not -- I have not done a separate risk assessment just for asbestos by itself, because I have not assumed that there is asbestos-only exposure.
Does that make sense?
But I do cite -- for example, I cite to some of the early literature on -- so this -- I guess where this opinion comes in is on hazard and warning. So in the warnings I talk about when it was known that asbestos was linked with cancer, because the warning standard is not causation proven but the identification of the potential. And so that is in my report on warnings, but that is not within my discussion of the weight of the evidence for risk assessment of the talc product.
Q. Okay.
A. Does that make sense?

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Q. Uh-huh.
For example, have you rendered an opinion about what dose of asbestos exposure would be necessary to cause ovarian cancer in an individual?
A. No, I have not formed that opinion at this time.
Q. Okay. Do you have an opinion about the background level of asbestos to which individuals are exposed with no increased risk of any type of cancer?
A. No, I do not have an opinion. I do believe others do, but I do not.
Q. Okay. You may have been asked some of these questions before, but I will keep them brief.
Have you ever published any articles that state that talc causes ovarian cancer?
A. No, I have not.
Q. Have you ever publicly expressed the opinion that talc increases the risk of ovarian cancer outside of literature?
A. No. My work has been in the -- in the courtroom.

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MS. BRANSCOME: I think we can take a break.
VIDEOGRAPHER: We are going off the record at 2:57 p.m.
(Off the record at 2:57 p.m.)
VIDEOGRAPHER: We are back on the record at 3:13 p.m.
MS. BRANSCOME: Dr. Plunkett, I have no more questions for you on behalf of Johnson & Johnson, subject to your counsel doing a direct of any kind.
THE WITNESS: Sure. Thank you.
EXAMINATION
QUESTIONS BY MS. BOCKUS:
Q. Good afternoon, Dr. Plunkett. You and I have met before. My name is Jane Bockus, and as you know, I represent Imerys in this case.
A. Yes.
Q. Correct?
I want to go back to just touch briefly on a couple of issues that have already been addressed.
Would you agree that IARC has

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not classified any of the heavy metals that you've identified in your MDL report as carcinogenic to the ovary?
A. So the answer is I'd have to look. I don't recall that, but I'd have to look to confirm.
Q. Okay.
A. That's the answer I believe I gave a few minutes ago, yes.
Q. So if I look at the IARC website, then I can confirm whether or not they have identified any of those as carcinogenic to the ovary?
A. Not so much the web -- well, the website or the actual documents. I think I would actually point you to the actual monograph --
Q. To the monograph.
A. -- because there may be evidence in there of ovarian cancer as being seen in studies. And I'd have to go look.
Q. Okay. That was not part of your consideration here, correct?
A. So ovarian cancer is part of my consideration, but I didn't -- in this part

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of my evaluation I'm trying to -- trying to describe these metals. And this is really about mechanism of biologic plausibility and the fact that these two things can go together, and then the concept of additivity is they're on hazard. The idea if you have a cancer hazard generally and you have similar mode of action, regardless of the tissue, you would be expected to have a potential additive effect when you do a risk assessment.
So that's my use of that data, which is why I didn't do a separate ovarian cancer assessment for each of the each constituents but just on powder.
Q. And you discuss that topic on page 47, paragraph 68, of your report, correct, the -- whether there's an additive effect?
And you cite to Casarett and Doull. I don't know if I'm pronouncing those names correctly.
A. I'm sorry, on what page?
Q. I'm on page 47, paragraph 68.
A. Okay. Sorry. I should know

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where it is, but...
Okay. I'm there, yes. Okay.
Yes, I do cite to a chapter in Casarett and Doull, yes.
Q. Okay. And Casarett and Doull is a resource that you cite to for a couple of different toxicological principles that you discuss in your -- in your report, correct?
A. Yes, because it's one of the most well-recognized textbooks that is used across different either universities or schools or even in regulatory agencies.
I would also say I cite EPA 2000 there. I'm not citing just Casarett, but I am citing Casarett as well as an EPA guidance document.
Q. In Casarett and Doull, do they actually discuss talcum powder in Chapter 2, or is it more just the concept of the potential of the effects when you have two different chemicals that you're exposed to at once or three or four?
A. It's the latter. It's the -- because you'll notice the title is

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"Principles of Toxicology," so it's the general chapter teaching principles for risk assessment and toxicology as used in risk assessment.
Q. And whether there is an additive effect of, say, talc and nickel, that's something that an experiment could be designed to study, correct?
MS. PARFITT: Objection.
THE WITNESS: If you're talking generally for cancer and not worried about the issue of ovarian cancer, if you're talking about cancer, like doing an inhalation experiment to look what happens to the lung, that you could do.
The problem with the animal studies and ovarian cancer due to perineal exposure is it's very difficult to understand how you design a study to expose the animals that way reliably in the way that humans are exposed.
But generally you could study -- you might even be able to do

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a genetically susceptible mouse study to hurry the process along to look at, but you might not be able to do it through perineal exposure. You might have to do it through another route such as either inhalation or maybe even you could -- you could look at it through intraperitoneal injections, for example.
QUESTIONS BY MS. BOCKUS:
Q. Well, and what the textbook talks about is the fact that you need to study it to find out whether the effects are additive, whether the effects are something that multiply the risk, you know, so that the two together are greater than either one alone, or do the effects offset each other and reduce the risk, correct?
A. That is discussed there --
MS. PARFITT: Objection.
THE WITNESS: -- which is why I've cited the EPA document. Because the EPA document addresses the issue of mixtures, and this is the issue of mode of action. If you have chemicals

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that you're looking at on the issue of additivity or no effect, you will -- you look at that issue of how they're affecting the tissue and underlying mechanism.
But the only way to look at the magnitude absolutely of how the risk would change is by doing an experiment. That is true.
QUESTIONS BY MS. BOCKUS:
Q. And to your knowledge, that experiment has never been done; is that correct?
A. I can't guarantee that it's only been done for nickel and talc alone, but I would -- I would state that based on -- there are studies out there that have been done where they've used the body powder that we know have metals -- a variety of things within it that are not just platy talc, but those experiments are that kind of data.
But as far as gathering dose-response information or teasing out individual components, that is not available.
Q. Do you agree that dose response

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is the fundamental principle of toxicology that underpins the effects that chemicals can have on living organisms?
A. When you're talking general toxicology, yes, I think it's talked about in the textbook.
Q. And you agree that it is the dose of the chemical and the pattern of exposure that determines whether a chemical produces an adverse effect on an organism, not simply the presence of the chemical?
A. For a typical dose-response relationship for non -- for nongenotoxic events, absolutely, I would agree that is probably true. And I don't mean nongeno -- noncancer events.
In the issue of cancer biology, some of those issues don't hold all the time. In other words, there are certain chemicals and certain ways of looking at cancer risk assessment where you can't assume where the threshold is or identify what a safe dose would be. But certainly I agree on the issue of noncancer risk assessment generally, or general end points of toxicity, that is true.

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Q. And again, do you agree that in general toxicology the effects that might be reported at high doses will not occur at lower doses if the concentration at the site of action falls below the threshold for toxicity?
A. Yes, that could -- that could be possible, yes.
Q. And do you agree that evidence-based toxicology and epidemiology dictates that the dose of the chemical is the critical factor when examining the risk posed by a chemical, not just its presence even in the human body?
A. I would say that's generally true, yes, which is why I have attempted to look at the dose-response relationship as well as the prevalence of the contact.
Q. And with regard to the human studies that you cite, would you agree that none of the studies that you cite in your report that have to do with migration of particles within the genital tract of the female involve applications to the perineum or outside of the genital tract?

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A. That is true with the exception of Parmley and Woodruff, which addresses this issue of --
MS. PARFITT: Objection.
THE WITNESS: Talks about the issue of exposure from the outside to the inside.
But the data that is collected with the different studies they have deposited at some point -- at some position within the vagina, that is true.
QUESTIONS BY MS. BOCKUS:
Q. And that is not how talc is deposited in women who use it regularly in their daily routine, correct?
MS. PARFITT: Objection. Misstates the evidence.
THE WITNESS: So I would say that depends on what women are doing. Perineal application, for example, application on the underwear, can lead to contact of the vaginal opening depending on the woman.
For example, a woman who has

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a -- had many children has a tract that is stretched. There, indeed, you can have more direct contact than you can with a very tight -- so I would say it depends on the woman and it depends on the situation.
But I do think it's generally accepted, based on my review of the literature, that there is the opportunity for exposure internally from perineal application.
QUESTIONS BY MS. BOCKUS:
Q. And if I understand what you testified to earlier today and yesterday, you don't have any data that would advise on -- out of the talc that is deposited in the underwear, what percentage of it makes it into the reproductive tract?
A. That's the data that's missing, that is true. And unfortunately, no one has done a study. It would be -- if there was a way to do that, it would be interesting to do that. I just don't see how you design that study, especially knowing the hazard of talc at this point. I think that would be a

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difficult study to get approval for.
Q. And do you have an opinion as to whether it is even correct that each day that a woman uses talc in her underwear, that some of the talc makes its way to the ovary?
MS. PARFITT: Objection. Form.
THE WITNESS: Have I -- can I quantify that?
No, I haven't quantified it. I think I got asked that earlier. I can't quantify the amount that gets there. Or, I'm sorry, I may have misheard the start of your question. I apologize.
QUESTIONS BY MS. BOCKUS:
Q. Yeah, I'm really asking: Do you have an opinion as to whether it happens every single time a woman applies talc to her perineal area? Does some of that talc make it to her ovary?
MR. MEADOWS: Objection.
MS. PARFITT: Objection.
THE WITNESS: I don't think I stated it quite that way, but certainly I think the opportunity is

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there with every application. And of course it would depend upon the amount of time that the contact may be in place. But the opportunity is there.
So, for example, if you applied it to your underwear and 30 minutes later you go to the bathroom, it's very possible that you will have wiped away, and so that that application may have taken an opportunity away. But I do believe that the opportunity is there based on the literature I have seen.
And so I haven't formed the opinion, though, that it's absolutely every time. My opinion, I think, is based on the fact that I believe that there is data to indicate that exposure occurs, and that with routine, continual habit, sort of a habit exposure, that indeed that there was some migration that occurs.
QUESTIONS BY MS. BOCKUS:
Q. And is it fair to say that you don't have an opinion as to whether that

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migration occurs every day, once a week, once a month?
MS. PARFITT: Objection. Form.
THE WITNESS: I haven't formulated my point -- my opinion quite that way; however, I do believe that it is something that is going to happen routinely with exposure. I do believe that migration is something that is going on routinely with application.
So with applications, I do believe that that is, but I can't tell you that this amount has migrated on this particular day with this particular application, no. That -- the data that we have collected is not there to allow us to do that.
QUESTIONS BY MS. BOCKUS:
Q. How do you define the word "routinely" as you're using it in that answer?
A. So that would be the idea of repeated exposures, you know, within a week, within a month, within a year. So not --

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routine to me would not be -- would not be applying it once a month one month, waiting six months, doing it again, and then not doing it until the next year.
Again, it's the idea -- some people may -- routine may be during the hot season of the year, they're routinely getting daily exposures when it's warm, and during the cold weather not applying. But then the next year doing -- that's a routine for them and their habits based on their pattern of exposure.
Again, we know that talc, when it -- when it migrates and gets into the body, we have data to show that it is -- it is able to persist in the body. The fact that you may have not been exposed for three months because it was cold doesn't mean that you -- that that changes the fact that you're still at risk with additional exposures the next -- the next time that that habit becomes -- comes into place.
So I think there's multiple exposure patterns that are possible, but when I use routine, it's something that people are

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doing throughout their -- a period of their life. And so it would be something that happens either on a weekly basis for a good part of the year. I haven't defined it with a particular number, though, no.

Q. And my question had to do with out of the number of times a given woman -- or an average woman uses talc, what percentage of the time does talc make its way into her reproductive tract?

A. So I don't think that anybody -- anybody can point to a piece of data that tells you that, but, again, it's based upon the anatomy, I would expect there to be the potential each time it's applied.

And on your question on routine, when I'm talking routine, I'm looking at not just frequency but also duration. So when I'm talking about dose, it's the fact that they do it on a repeated basis for a number of -- a period of years as well.

That's what the data shows in the human studies. It's not something, again, that may have been done routinely for

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one year, but it does appear to be something that's done more -- longer term than that.

But we can't give a number. We have no threshold. We don't know exactly what that minimum number is.

Q. Do you think that the minimum number is greater than a year?

MS. PARFITT: Objection. Form.

THE WITNESS: I haven't formed that opinion, no.

QUESTIONS BY MS. BOCKUS:

Q. Do you think it's greater than a month?

MR. MEADOWS: Objection.

THE WITNESS: Greater than a month?

QUESTIONS BY MS. BOCKUS:

Q. Yes.

A. One month in their life?

Q. One month in their life, where they're using it every day for a month.

A. So I haven't formed that opinion at this point in time, but I'd say it's more likely to occur when you do it more than a month. But I haven't formed an

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opinion on a set number, no. I can't -- can't point you a specific number.

I'm not doing case-specific, so I've not looked at any of those pieces of information for any given plaintiff.

Q. And I'm just trying to get the threshold.

A. Uh-huh.

Q. As I understand it, that is part of a toxicological evaluation, is the threshold below which there's not an issue.

So I think you've said you don't know if it's less than a year, but you think it's more likely than not that it's greater than one month.

MR. MEADOWS: Objection.

QUESTIONS BY MS. BOCKUS:

Q. Is that fair?

A. No, that's not exactly what I'm saying. I'm saying we don't know the threshold. So as a result, I'm not of the opinion that it absolutely can't -- it only has to be this long.

What I'm saying to you is per general principles of toxicology and based on

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the human data that we have, it indicates that it's more frequent than just one month, but I can't tell you that it's absolutely not possible.

That's where -- I do think when you're talking about those kinds of patterns, that's a case-specific issue for individuals, because I think that would have to be considered for each individual. But certainly as a toxicologist, I'm using the words "routine," "repeated," "longer duration," "chronic exposure." And when I defined "chronic" earlier, I talked about years of exposure versus just one month.

That would be consistent with what I have said, yes, but I'm not -- I -- I certainly don't want to rule out that there couldn't be somebody out there that could show something different, because it may very well be that there are people that you can identify with the presence of talc in their ovaries and all of their other case-specific things that could -- could make that pattern a -- make someone be able to draw a case-specific, reliable conclusion.

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But that's not my role. I don't do case-specific.
Q. And I am simply trying to get the parameters of your opinions with regard to the amount of talc use one would need to have before you would feel comfortable -- well, that in your opinion would be sufficient to create a toxic environment.
MR. MEADOWS: Objection.
THE WITNESS: Well, that's a different question. So toxic environment could be with a much shorter time exposure, okay?
QUESTIONS BY MS. BOCKUS:
Q. Right.
A. So but if you're talking about -- the opinion that I have formed has to do with an increased risk of ovarian cancer. So with that opinion, that's the description, I believe, I was giving this morning. It's the idea that the data that I've seen indicates that my opinion that perineal use of talc body powder products increases your risk for ovarian cancer above that background level that you know exists.

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That opinion is based on data that is -- is -- the supporting data would indicate that it has to be a habit, routine, a chronic exposure. And so as a toxicologist, I've tried to put that in context.
I don't know what else to tell you. That's the opinions I have formed to date.
Q. A chronic -- a habit, routine, a chronic exposure for years?
A. Well, chronic --
MR. MEADOWS: Objection.
THE WITNESS: -- is defined as years, typically, by a toxicologist, and so that's what I -- that's what I told you.
QUESTIONS BY MS. BOCKUS:
Q. Shifting to your regulatory opinions, you would agree that Imerys is a raw material supplier to J&J; is that correct?
MR. MEADOWS: Objection.
THE WITNESS: I would call them an ingredient supplier, yes.

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QUESTIONS BY MS. BOCKUS:
Q. Okay. An ingredient supplier.
And you agree that Imerys does not sell any products to the general public, correct?
MR. MEADOWS: Objection.
THE WITNESS: I don't know that's definitely true, but I'm not aware that they do.
QUESTIONS BY MS. BOCKUS:
Q. And what Imerys supplies to Johnson & Johnson is not a finished cosmetic that is ready to be sold on the market, correct?
MR. MEADOWS: Objection.
MS. PARFITT: Objection.
THE WITNESS: I don't know that I can answer that except in the context of Johnson & Johnson's baby powder, SHOWER TO SHOWER® and Shimmer, it's my understanding that Johnson & Johnson mixes -- has some fragrance added to the talc.
I don't believe Imerys does that, but I don't know for sure.

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So based on what I know -- I'm telling you what I know, and I would call them, again, an ingredient supplier, and I would call Johnson & Johnson a cosmetic manufacturer.
Does that answer the question?
QUESTIONS BY MS. BOCKUS:
Q. It does.
Would you agree that the minerals that you have identified in your report, that the documents that you have seen, would classify their -- to the extent that they are ever in the powder, that they're trace ingredients?
MS. PARFITT: Objection.
MR. MEADOWS: Objection.
THE WITNESS: So which ingredients are you referring to?
So some of the metals, no, are not trace ingredients.
Are you talking about the -- are you talking about the -- like the presence of tremolite or the presence of chrysotile --

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QUESTIONS BY MS. BOCKUS:
Q. No. No, I'm sorry. I'm talking about the three metals that you identify in your report. Those are trace elements that are -- that are sometimes detected in the studies of the -- of the talc.
MR. MEADOWS: Objection.
THE WITNESS: It's not how I would say it. I would say they're heavy metal components that are naturally occurring within the product that are sometimes -- sometimes detectable at levels that are reported as trace based on the detection limit within the analysis, but at other times they're not listed as trace. They're actually listed with a specific amount.
So that's what -- how I would define what I call trace. Usually that's how it will be reported in the lab, trace, which means below the limit of quantification, but it's there. You're detecting it.

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I would agree that -- that there are other descriptions of heavy metals in the heavy metal literature that talk about trace amounts being found in -- naturally occurring in food, for example, and I agree that that does occur. But in the case of this product, we actually have often -- we actually have a -- a limit that is set for acceptability in the specification.
And so I would think it's more proper to call it a level of the heavy metal that is allowable by the purity specifications set by the product. And sometimes those levels may be above, and most of the times those levels are below, which is why it's cleared. Because I've seen some analyses where different products may have been, I guess, turned away or considered not acceptable based on the analysis of certain types of minerals or metals.

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QUESTIONS BY MS. BOCKUS:
Q. Have you seen any studies where women's blood has reflected the presence of nickel or cobalt or chromium?
MR. MEADOWS: Objection.
QUESTIONS BY MS. BOCKUS:
Q. Who are parts of these studies -- these ovarian cancer studies?
MR. MEADOWS: Objection.
THE WITNESS: The epidemiological literature you're asking me?
QUESTIONS BY MS. BOCKUS:
Q. Yes, ma'am.
A. It's possible in the Nurses' Health Study that we can go to that, because I know they do collect some heavy metal levels. I've done that for other clients on other issues.
Most of the others, I doubt that we have heavy metal levels in blood. But certainly there are levels of heavy metal in blood, especially things like lead, for example, that we have very limited capacity to eliminate.

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So whether or not you carry around a significant body burden of a heavy metal in your blood is somewhat driven by the exposure pattern you get. It's something that's commonly -- or can you excrete it quickly or not. So...
Q. And are you familiar with any studies that have suggested that the use of body powders leads to a heavy burden of nickel, chromium or cobalt in the blood?
A. So I have not seen such analysis done, no, I have not.
Q. In paragraph 67 of your report, which is on page 46 -- I'm sorry, on -- oh, I'm sorry. Paragraph 64, I apologize.
A. No. No, that's fine.
Q. It's on page 44.
You cite to two abstracts --
A. Yes.
Q. -- one by Fletcher and one by Fletcher and Saed.
Do you consider these abstracts to be reliable sources of data?
A. They're not as reliable at all as a peer-reviewed article. So there's a

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difference in the weight you give an abstract, absolutely.

However, knowing the papers that Dr. Saed has actually published in the peer-reviewed literature, I have -- I have mentioned them in here because I do believe that they are -- they are pieces of information that are highly relevant to some of the issues raised in other cellular studies, and so that's why they're here. But certainly I do not give them the same weight as in my assessment of overall risk.

And I would say that I had the same opinions on risk before I had these studies. Because in my original reports, obviously, I have gone further than risk and talked about cause, and I didn't have the Fletcher studies.

The Fletcher studies are more on the issue of biologic plausibility and mechanism versus being important underpinnings, for example, for a hazard assessment.

Q. Is there any way that someone reading your report could tell that you

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attribute less weight to the abstracts by Saed and Fletcher just by reading your report?

MR. MEADOWS: Objection.

THE WITNESS: I don't know if they could or not. Hopefully they would based upon where they appear in the report. They're not cited a lot of other places, but they certainly are cited.

So that's why I'm here today, though. You're asking me these questions; I'm telling you. That's how I look at these studies. That's all I can say.

I haven't -- I haven't, certainly, as I've told you, given things numerical weight throughout my report.

QUESTIONS BY MS. BOCKUS:

Q. Looking at paragraph 118...

Well, when you were preparing your report, were you careful with the language that you used in it to be precise and accurate?

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A. I attempted to do that. I can't tell that you there isn't something in here I've missed. But, yes, I read this report six or seven times before I finalized it, trying to make sure that the language I was using was an accurate reflection of the opinion I'm expressing.

But it's possible, if you want to point to something that you want to ask me about, I can tell you whether or not that was something that I would change.

Q. So on page 77, paragraph 118 in the middle of it, you say, "Based on the knowledge available by the 1950s, talc body powders manufactured and sold by Imerys and Johnson & Johnson."

And that's the question that I have for you.

A. I see what you're saying.

Q. Was Imerys selling anything to Johnson & Johnson in the 1950s?

MR. MEADOWS: Objection.

THE WITNESS: I'm thinking. It's possible they did not. That may be true.

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QUESTIONS BY MS. BOCKUS:

Q. Well, and actually --

A. You know what? When I wrote this sentence, I assumed that they did, but if that is not true, then certainly this sentence should be just Johnson & Johnson.

Q. Well, earlier in your report, in a footnote you indicate that Imerys began supplying talc to Johnson & Johnson in 1989 or the late 1980s.

Do you remember making that notation?

A. So let me look. So if that's an inconsistency, then that should change. Let me look.

Q. And that's all I want to know, if it's an inconsistency, should it change.

A. If it is an inconsistency -- certainly if Imerys was not selling talc to Johnson & Johnson in 19 -- the 1950s, then -- then certainly Johnson & Johnson's products would not -- would not be affected by Imerys' activity.

However, if Imerys is selling talc to anyone that makes a consumer product

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in the 1950s, then -- or a precursor company to Imerys is making talc that's selling for body powder to somebody other than Johnson & Johnson, then that opinion would still hold.

So -- but I certainly agree, I think I -- you're right, I think I have a statement about the link between the two in '89. So in that case, then certainly the -- the link here would be related to Johnson & Johnson's products.

Q. Okay. Yeah.

A. Whether or not -- if they weren't sourced from Imerys, then that's a separate duty on a product, not this product.

Q. If you look on the bottom of page 7, I think you'll see the footnote I was referencing.

And with regard to your last answer, you don't have any information as to whether Imerys existed and, if it did, what -- who its customers were in 1950s, correct?

A. I don't believe I do, no.

MS. BOCKUS: I think that's all that I have. Thank you.

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MR. LOCKE: I've got a few questions.

EXAMINATION

QUESTIONS BY MR. LOCKE:

Q. Doctor, my name's Tom Locke. I represent the Personal Care Products Council. We met a couple of times before, I think.

A. I apologize, I don't recall your name at least. The face looked familiar, though. I apologize.

Q. I try to maintain a low profile.

I have relatively few questions. I wanted to ask you overall about your opinion.

Would you agree that reasonable scientists can disagree with your opinion that talc increases the risk of ovarian cancer?

A. I'd say I wouldn't say it quite that way. I'd say that I agree that scientists can disagree on conclusions they draw, depending on the -- depending on the way that they have assessed.

So certainly based on a

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complete assessment the way I did, then I would agree that other people could come to a different conclusion, absolutely.

So I think it depends what you mean by "reasonable scientist." But I would agree that individuals can look at the same body of data and, based on their judgment and experience, based on looking at that same body of data, could come to a different conclusion, yes. That's true.

Q. You've been involved in this talc litigation for at least a couple of years, right?

A. Yes.

Q. And you know that various defendants have offered experts who disagree with your conclusions, right?

A. Some of my conclusions, yes. I don't know that there is somebody that's in the litigation that does exactly what I do across all the opinions I've expressed, but, yes, certain parts of my opinions there are other experts I'm aware of, yes.

Q. Well, they -- you're aware that there are defense experts who disagree with

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your opinion that talc increases the risk of ovarian cancer; is that correct?

A. Yes, I -- I am aware of that fact.

Q. And in your review of the records that go back or the scientific materials that go back 35 years or more, you've seen that there's disagreement regarding that issue; is that correct?

A. So what documents are you referring to? Are you asking me about a specific -- just the published medical literature? Are you asking about documents like internal company documents, reviews by others? What are you asking me about?

Q. Well, let's focus on the published medical literature.

There are scientists who have disagreed with your opinion; is that correct?

MS. PARFITT: Objection.

THE WITNESS: I'm not aware of a paper in the published medical literature that has done the exact assessment I have done.

So I am aware of the fact,

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however, that there are individual papers by scientists that, for example, have concluded that there is no association between exposure to talc perineally and ovarian cancer, yes. Individual papers, I am aware of that, but that's different than what I have done.

QUESTIONS BY MR. LOCKE:

Q. Let me just ask you about what you were requested to do on behalf of plaintiff's counsel.

Plaintiff's counsel asked you to provide opinions related to the human health hazards posed by exposure to talcum powder products and how those hazards relate to the regulatory requirements for marketing cosmetic ingredients and cosmetic products in the United States; is that correct?

MR. MEADOWS: Objection.

THE WITNESS: I didn't write that, but that sounds like an accurate reflection of what -- what we -- what I have done at least in parts of my report, yes.

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QUESTIONS BY MR. LOCKE:

Q. Well, if you look at your report, I think you go to part where you were asked to provide -- and I just pulled it from what you said.

A. So I did write it, I apologize. It didn't sound like me.

Q. It started with "to provide opinions related to the human health hazards" and so forth, so I just wanted to make sure we're clear on that.

A. Sure.

Q. So does that sound right in terms of what you were asked to do?

A. I said I -- certainly those are the kinds of things that I was definitely asked to do. I was asked to do two basic -- two basic things, which was having to do with toxicology and risk assessment, and then a separate issue related to regulatory concerns.

So, yes, those are the two basic, I guess, buckets of information and documents that I reviewed and opinions I've expressed, and I think that's consistent with

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what I've been doing in the litigation.

Q. Okay. As to that second bucket, the US regulatory requirements for marketing cosmetic ingredients and products, that's not relevant to the scientific question whether talc may cause ovarian cancer; am I right?

A. No. I disagree with that based on the fact that a company that markets a cosmetic product is required to do a safety assessment. And if in that safety assessment issues relate to cancer or ovarian cancer and the use of talc, then those two things are related.

But I would agree that -- that doing a risk assessment like I've done is a separate issue from doing a safety assessment for a product, because there's actually even a lesser standard for an issue of looking at a safety assessment for a product versus actually forming the opinion that there is an increased risk of cancer with exposure to talc.

Q. Now, did IARC in 2006, did it look at the US regulatory process in

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considering whether talc may cause ovarian cancer?

MR. MEADOWS: Objection.

THE WITNESS: I don't think I understand what you mean. It's not a US regulatory process, no, if that's what you're asking me.

They have a -- they have a discussion of what the products are, which is part of the way they're sold. But I don't think they're discussing the duty of a company under the regulatory process, no, that's a separate issue.

QUESTIONS BY MR. LOCKE:

Q. So their analysis of whether talc may cause ovarian cancer, that's different than the analysis of whether a company may have a duty, whatever that duty may be?

MR. MEADOWS: Objection.

THE WITNESS: It's a different process, absolutely. IARC is a separate, independent body that does an assessment looking at the issue of

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cancer hazard and looking at whether or not there is sufficient evidence to categorize that hazard, whereas a duty of a company under the regulatory situation is broader than just cancer hazard; it's a whole different thing. It's what you do internally before you market a product. Totally different.

And so certainly when I -- that's why I have separate sections in my report, and that's why I even have -- I've had discussions about the difference between the regulatory standard for warning versus the assessment of risk that may be required in order to start to produce a -- identify a association or an increased risk or even if you did a causation analysis. Totally different type of exercise.

QUESTIONS BY MR. LOCKE:

Q. Do you first, in that exercise, look at the scientific issue of whether talc may cause ovarian cancer?

A. Are you asking me in either of

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these exercises?

Q. Well, let's say when you're getting to -- you mentioned the duty to warn. So if you're looking at the duty to warn, do you first have to look at does talc cause ovarian cancer?

MR. MEADOWS: Objection.

THE WITNESS: That's not the question you asked. No. I would argue, based on the regulations, if you look at the standard, the question is, is there evidence to indicate that there is a chance, there is a potential -- not that it does, but is there a potential for that type of hazard to be posed to consumers who use the product.

It's a possibility versus being a -- I'm taking it beyond possibility when I'm doing my assessment for increased risk. And I talked about that this morning, and I can't remember her last name. The Johnson -- I apologize. But I -- with Johnson & Johnson. I talked about

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this is a different assessment and different standard. It's a much lower standard on cosmetics for what needs to be done as far as warning.

Now, when a company comes and initiates a safety assessment on their product, before they even think about what am I going to warn, they should be doing a comprehensive assessment of safety based on what's available publicly, knowing what others have reported and then what data they've collected.

If they don't have data at all on the safety of the product, then the product has to say that. We don't know. We do not know if this product is safe. And that's one of the things that is allowed under FDA -- under FDA regulations as well.

But essentially some -- some assessment must be done to understand from the perspective of the company that this product is safe for consumers to use as -- under the

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directions of use.

So in the case of this, it would be a body powder being used on the body surface but also perineally because -- because that was an exposure pattern that was understood.

QUESTIONS BY MR. LOCKE:

Q. Okay. You described two different buckets. They're independent assessments; is that correct?

MR. MEADOWS: Objection.

THE WITNESS: Initially that's where I started, and now I'm talking two different duties. There's a duty to warn, but there's first a duty to collect information before you market it. It's your premarket safety assessment.

QUESTIONS BY MR. LOCKE:

Q. Okay. I'm not actually talking about the manufacturer's duty. I wanted to just first address your scientific analysis.

That's a separate question that led you to your opinion on the -- your opinion that talc increases the risk of

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ovarian cancer, correct?
MR. MEADOWS: Objection.
THE WITNESS: Yes, that's what I described. And I thought you were talking about duty of the company, and so I apologize. I didn't mean to go off on a tangent.
If you want to focus just on the risk assessment -- is that what you want to do? -- that's what I'm doing.
QUESTIONS BY MR. LOCKE:
Q. No, I just want to understand, those are two different things, though, right?
A. Those are two different -- those are two different tasks that I undertook, yes. I undertook a risk assessment task to form opinions based on what I can say about risk, and then I separately -- and I had done this earlier on the issue of warnings, looking at what do we know about the product and whether or not -- and when did we know it, and what should consumers have been warned about based on the

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safety information that was available over time.
Q. The risk assessment task, that's what you mean by your analysis that talc increases the risk of ovarian cancer?
A. That's correct.
Q. You could have stopped at that, but then you performed an additional task; is that right?
A. Well, actually, no, because the first task I actually started with was the regulatory task. When I first started getting involved in the litigation very -- before I wrote my first report, one of the first things I was looking at was the issue of the duty of the manufacturer to provide warnings.
And then after that, I expanded that role to be an inclusion as well of a causation analysis.
And then now I'm not doing a full causation analysis in this litigation, but I'm using essentially some of the same information to provide you with a description of a -- a health risk assessment, which was

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also sort of -- that's a piece along the way to doing a causation analysis, but it's not the same.
Q. Your opinion regarding the FDA's responsibilities and functions, that's not related to your opinion that talc may cause an increased risk in ovarian cancer; is that correct?
MR. MEADOWS: Objection.
THE WITNESS: I don't think that's true the way you're asking that question, because I don't know how you divorce the fact that as a -- in a regulatory assessment, if I identify cancer hazard, I have identified a duty to warn. That's certainly something that should be warned about when I understand that there's not only the potential, but I believe there's an increased risk.
But I would agree with you that in my report, I'm laying out for you even different bodies of information that -- as I step through it.
Does that make sense to you?

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QUESTIONS BY MR. LOCKE:
Q. Not really.
A. I'm sorry.
Q. I'm talking about your scientific analysis here, not your regulatory analysis.
To do your scientific analysis, you looked at scientific materials, right?
A. Yes, but I do the same thing for my regulatory analysis. That's why I'm confused. I -- to me they are connected.
But I would agree with you, I had an analysis. Let's just talk about that, my analysis on risk assessment and my opinions that I've expressed. Those are laid out in a separate section of my report, absolutely. So we could talk about that if you'd like.
Q. Well, I just want to understand, and I think I do now, that's a separate issue from your regulatory opinion?
A. It's not a separate issue. That's where I'm having trouble with your language.
It's a separate task because,

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for example, I may have only been asked, but I wasn't, to just describe whether or not, as a human risk assessor and toxicologist, there is a hazard or a risk posed by the product, and I could stop there.

But I was asked, based on -- based on my experience working in the area of regulatory toxicology but also on regulatory issues for clients where I give advice, I was asked to look at how does that scientific information impact what the company should be doing.

And so that's -- that's why I'm saying you can't divorce them, because the warning issue I'm talking about is intimately tied into the human health risk assessment results.

Q. So do you consider yourself primarily here as a warning expert?

MR. MEADOWS: Objection.

THE WITNESS: I consider that one of my roles, yes, absolutely.

It depends upon how individual cases, individual attorneys, will -- will ask -- decide to use me. For

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example, I have been used in one trial to only talk about the toxicology. Other trials, I've talked about toxicology as well as regulatory issues. So I think it just depends on the case.

In the MDL, I am prepared, however, to come to talk at a trial on the regulatory system that guides cosmetics as well as provide opinions that talk about what are the hazards of talc, what is the toxicology of talc, what do -- how can you be exposed to talc, that migration issue, and then my opinions about whether or not I believe that there is an increased risk of ovarian cancer.

So I would be -- be prepared to talk about both of those things. That's why I said I do think I'm a little different than some of the other experts that you may encounter, for example, in the defense side, where someone may just do regulatory or somebody may just do toxicology.

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But I practice in both those areas in my consulting practice and in my experience.

QUESTIONS BY MR. LOCKE:

Q. Let me ask you a few questions about your cosmetic ingredient review statements, CIR.

We can agree to call it that, right?

A. Yes, that's fine.

Q. In parts of your report, you cite the CIR as an authoritative source on cosmetic ingredients; is that correct?

A. So where are you looking at, the background information on the CIR?

Yes, they certainly are a source of information that FDA relies upon as far as assessments, yes, that's true.

Q. Well, and on page -- or paragraph 35, page 23, you cite to the CIR on, for example, chemicals purportedly in cosmetics. You have a footnote there.

A. So --

Q. I believe it's footnote 31.

A. Yes, I have looked at -- looked

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at the CIR as a source of information because many of the chemicals, many of the ingredients within the fragrance of Johnson & Johnson, the only available information may be found within the CIR that's publicly available.

Q. And you rely on the report of Dr. Cralley; is that correct?

MR. MEADOWS: Objection.

MS. PARFITT: Objection.

QUESTIONS BY MR. LOCKE:

Q. You reference Appendix D to your report. I believe if you stay on the same page you'll see that, the same paragraph.

A. I wouldn't say I rely on the report of Dr. Cralley because I form my opinions independent of Dr. Cralley, but certainly his -- I believe if you go to his reports, his report is supportive of my opinions in this area.

Q. Did you read his report?

A. I have read it now, but I did not read it before I -- before I formed my opinions in this particular paragraph, yes.

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Q. I'm a little confused because you're citing to his report.
You read it or you didn't read it before you wrote this paragraph?
A. I read it before I wrote the paragraph. I didn't read it before I had formed the opinion. Do you understand what I'm saying?
I did my review of the irritant chemicals independently before I looked at Dr. Cralley's report. So I had formed the opinion that -- of the chemicals I had searched for that this is what I identified. And that's what this is talking about, right?
I'm saying here that of the more than 100 chemicals included, over 70 percent are compounds linked with some level of irritant hazard. That was done on my own.
Then, if you go to look at Dr. Cralley's report, I cite it here because it's consistent. That is, his report provides support additionally for the statement I'm making.
So I'm not relying on his

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conclusions to make my opinion, but it's certainly -- I am citing it here as it being a piece of evidence that is consistent with my opinions.
Q. Sorry, I seem to have messed up my microphone. I'll try to hold it for a little bit then.
Do you disagree with Dr. Cralley's report?
A. I have not formed an opinion that I agree or disagree. He -- with his -- I believe he has information that is consistent with the opinion I'm expressing in the sentence, however.
Q. And do you know that Dr. Cralley repeatedly cites to the CIR as an authoritative source regarding cosmetic ingredients?
A. I don't know that he uses that exact language, but he does cite to it, yes, in his report. Certainly he does.
Q. More than 20 times, right?
A. That, I have not counted. I can't tell you that. But he does, just like I do, as a source of information when there

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is no other source available.
Q. Okay. In your report you state that the CIR process is administered independent of the FDA.
But the FDA is on the CIR steering committee; is that correct?
A. That is correct.
Q. You don't mention that in your report, although you mention others who were on the CIR steering committee, correct?
A. Yes, there's a paragraph where I talk about others, yes.
Q. But you don't mention that the FDA is on the steering committee?
A. I believe I -- I believe I've been asked that question before, and I said yes, but certainly in this report I don't believe I state that, that is true.
Q. CIR solicits input from the public; is that correct?
MS. PARFITT: Objection.
THE WITNESS: I would say they solicit input from industry, yes.
QUESTIONS BY MR. LOCKE:
Q. Well --

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A. But they -- and they do have a public comment period, which is mainly input from industry.
But I agree that they do -- and if what you're referring to is a public comment period, yes, there is that for the documents.
Q. You can go on the website and see what ingredients CIR is going to review, right?
A. Yes, you can.
Q. Have you done that?
A. Yes, I've done it many times before.
Q. Okay. And did you submit comments on talc in 2012?
A. No, I did not.
Q. Okay. You could -- the public can submit comments many times during the process of an ingredient review; is that correct?
A. There are different -- different stages of the draft document. Is that what you're asking me? Yes, that can be done.

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Q. Well, even before it's a draft, CIR is soliciting information about the ingredient to include in the initial materials provided to the expert panel; isn't that correct?
A. Technically I believe that is true, but I would disagree that that is something that happens routinely. But I would agree that -- I would say technically you may be -- that is something that could occur, yes, but that is not the situation, for example, in the case of talc.
Q. Why not?
A. Based upon what I have seen described as how the review was done, and that has to do with the testimony of different -- or different documents that I've reviewed and the testimony of individuals related to this document.
Q. Well, Dr. Cramer could have submitted comments to the CIR regarding talc, couldn't he?
MR. MEADOWS: Objection.
MS. PARFITT: Objection.
THE WITNESS: You'd have to ask

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Dr. Cramer if he was aware that they were reviewing it. I can't answer that for Dr. Cramer.
But if he was aware of it, certainly -- if you're aware of the process going on and the timing of it, certainly you can submit comments. I'm not disagreeing with you on that. That is true.
QUESTIONS BY MR. LOCKE:
Q. CIR publishes in advance what it's going to review; isn't that correct?
A. What is coming up for review?
Q. Yes.
A. Yes, things that are proposed for the next meeting, yes, that's true.
Q. And you could submit comments to the first draft of the CIR report; isn't that correct?
A. I would agree that that is possible to happen, yes.
Q. And you can submit comments before the final report is drafted, correct?
A. Yes, as long as it's still in draft form, yes, those comments can be

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submitted.
Q. And CIR meetings are open to the public, right?
A. That is true, they are open to the public, but in my experience it -- they are not meetings that are heavily attended by the public but indeed are -- tend to be meetings attended by industry stakeholders within the ingredients that are being reviewed.
Q. You know Mr. Steinberg here. He was a plaintiff's expert for a while?
A. I don't know him personally, but I know his name and I know he was a plaintiff's expert, yes.
Q. You know he attended the talc meeting, right?
A. Yes, I believe he was working with indus -- he works with industry, so I believe indeed he did attend that meeting.
Q. You're not claiming he was working with any industry member regarding talc, are you?
A. That's not what I stated. I know he's a consultant to the cosmetic

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industry, so it doesn't surprise me. And I believe he lives in the area, so it doesn't surprise me that he attended.
I haven't spoken to him about any of that, though, so I have no specific details of that.
Q. Transcripts of the meeting are available to the public, right?
A. You can download the transcripts, yes.
Q. They're on the website?
A. That's what I said. You can download. I'm sorry.
Q. Okay.
A. Yes, you can download them from the website.
Q. Did you submit comments to the CIR regarding talc?
A. No, I did not.
Q. Why not?
A. I wasn't aware of the process that was going on in the draft form at the time.
Q. Why is that?
A. I was not following the CIR for

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talc at that particular time. I have a lot of other clients and a lot of other issues that go on on a routine basis, and I -- I literally would not have time to follow every assessment they do, considering that they do thousands of chemicals.

Q. Did you know of the CIR prior to your retention by plaintiff's counsel?

A. Yes. In fact, I -- one of the journals that I receive, International Journal of Toxicology, maybe, publishes many of their safety assessments. So I certainly am, yes.

I was aware -- when I was at Eviron, I was aware of the existence of CIR.

Q. Have you ever provided prior to this litigation -- and by "this litigation" I mean any aspect of the talc litigation -- an expert opinion on cosmetics' ingredients?

A. You're asking me in any other litigation on a cosmetic ingredient?

I'm thinking back to the cases I've worked on. Not as a -- not as a testifying expert.

At Eviron, though, we worked on

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litigation involving cosmetic ingredients, thought I was not the testifying expert.

Q. In your report you talk about the percentage of -- or the number of ingredients that the CIR listed as unsafe.

Do you recall that?

A. Yes. I mean, if you want me to verify the number, I need to go there. But, yes.

Q. You don't mention that CIR has put limitations on approximately 50 percent of the ingredients that it has reviewed, do you?

A. I don't mention that, but they do. They have -- they have -- when they have a statement about safety, they will -- they will often talk about the limitations from the safe use based on either concentration or even maybe route of exposure, that is true.

Q. Why don't you do that? Why didn't you include that in your report?

A. No particular reason. I mean, the point I'm trying to make is really the workload that's going on here and the impossibility of the task of providing the

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same level of review of any of these ingredients as can be provided -- as was provided by the IARC.

And so, again, that's one of the comparisons I'm doing. I'm talking about the difference in the time, the effort, the difference in the independence of the reviews. And so that -- when I'm talking about, those numbers, that's what I'm focusing on. I'm focusing on the fact that you have so many reviews in a very short period of time, with a one-expert panel, it's impossible for that level of analysis and review to be anywhere near what IARC panels do, and also nowhere near the level of review that I have done based on the number of documents that I have analyzed and looked at. So it's a different type of review.

Q. Let me ask you a few questions because you have criticized the panel.

You would agree with that, correct?

A. Yes. Oh, absolutely. This particular analysis I have. I have made some general criticisms of the overall process,

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and then I made some specific criticisms of this particular review.

Q. And one of your criticisms is that the CIR -- I think you said two CIR expert panelists had conflicts of interest; is that correct?

A. Yes, that -- they did, that were not -- that were not -- I believe not understood even by Dr. Andersen at that time. I think these are things brought up to him that he was not aware of.

Q. All right. Now, you read his testimony in one of the trials in California, right?

A. Yes, that's the -- in fact, that's the source of the information where I'm citing to those names of those individuals. I think I refer to that, his trial testimony.

Q. And didn't he, though, say, well, he didn't view it as a conflict of interest because the money wasn't going to them personally, it was going to their organizations?

A. He did make that statement,

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yes.
Q. And you disagree with that statement?
A. I don't -- I mean, his testimony is what it is.
Are you asking me do I disagree that that's a conflict of interest?
I disagree that you shouldn't disclose that as a potential conflict in the documents that are produced, just like I do when I write an article and I disclose that I've had funding. I don't say what the funding specifically paid for, but I've had funding or support from this industry individual or that industry individual. It's -- it's something that just is about transparency.
Q. So when you write articles, you say that you've been paid a lot of money by plaintiffs' lawyers?
MR. MEADOWS: Objection.
MS. PARFITT: Objection.
THE WITNESS: Well, I haven't written an article that overlaps with an issue that I've addressed in

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plaintiffs' litigation, but I certainly have given my conflict of interest statements that relate to the issue in the article.
I do that -- I've done that with -- on my work -- several of my -- several of my assessments talking about risks of pesticides. I've done it with the work that I've done that that's been sort of, I guess, policy-type work on behalf of the American Chemistry Council.
So absolutely I do.
QUESTIONS BY MR. LOCKE:
Q. Okay. You don't think it's relevant that you receive 50 percent of your money solely from plaintiffs' products liability lawyers?
MR. MEADOWS: Objection.
MS. PARFITT: Objection. Form.
THE WITNESS: If it has nothing to do with the issue that I'm addressing in the paper, no, I do not think that.
But when you're accepting money

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from an industry or a company that has to do with the issue you're looking at, yes, a conflict -- a conflict of interest absolutely needs to be described.
QUESTIONS BY MR. LOCKE:
Q. And that would -- well, let me just ask you: You're not an ethicist, are you?
A. No, I'm not trained as an ethicist.
Q. And you're not a lawyer, are you?
A. Well, no, but I have passed the patent bar, but I'm not trained as a lawyer.
Q. That doesn't make you an ethicist, right?
A. No, it does not.
Q. Okay. Let's talk about one of the people you criticized, Dr. Wilma Bergfeld.
Did you know she was the first woman who was the president -- to be the president of the American Academy of Dermatology?

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A. No, I don't know her personally, so, no, I did not know that.
Q. Did you investigate her at all when you criticized her?
A. I wasn't criticizing her, I was criticizing the CIR process for failing to disclose the conflicts of interest of individuals that were involved in their assessment.
I certainly am not giving personal criticism to either of those individuals.
Q. You would agree that the American Academy of Dermatology is a reputable organization?
A. I haven't formed an opinion one way or the other; however, I'm aware of them, and certainly I know individuals that are members of it, yes.
Q. Are those individuals reputable people?
MS. PARFITT: Objection.
THE WITNESS: They are people that practice medicine that certainly I would go see. I mean, you're asking

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me if I formed a very specific opinion about them as individuals, and I haven't done that.
QUESTIONS BY MR. LOCKE:
Q. Do you have any reason to believe that the American Academy of Dermatology is disreputable?
A. No. Again, I haven't formed an opinion one way or the other. I'm aware of the organization, and it certainly is one that is -- has within its members a number of people that I know that practice in dermatology.
Q. Did you know that Dr. Bergfeld was the first woman to be president of the Cleveland Academy of Medicine?
A. To the what? What was the first word?
Q. Cleveland Academy of Medicine?
A. No. Again, I'm not aware of her CV specifically, other than what may have been discussed -- it's possible her -- I know her affiliation will be listed in some of the documents as to where she is today, but I do not know her CV and her history.

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Q. Are you aware that she was the first president -- or she was a president of the American Society of Dermatopathology?
A. No. Same thing. If I'm not aware of her CV, I wouldn't know that.
Q. How about that she was the former chair to the FDA's drug -- FDA's Dermatology and Ophthalmology Advisory Committee?
A. Same answer. I don't know her CV, so I have no knowledge.
Q. Is it your opinion that Dr. Bergfeld was not qualified to chair the CIR panel that considered talc?
A. I don't think I formed that specific opinion. Instead, what I have -- the opinions I formed relate to the overall makeup of the panel that failed to include individuals with expertise that were -- that are really key to assessing the safety of talc. And that had to do with the issues of, as I discuss it, epidemiology -- oh, I'm sorry, I think I need to put this back -- period -- sorry. In the area of epidemiology is one that I talked about it specifically,

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and also gynecological -- gynecological sciences on the issue of migration.
Q. You're not a epidemiologist, are you?
A. Not by training. It's a tool I use all the time, but I'm not an epidemiologist by training.
Q. And panel members on the CIR, they might have used the same tool that you're using to form your opinion about talc, correct?
MR. MEADOWS: Objection.
THE WITNESS: Based on what I've reviewed from the minutes and the write-up, I would disagree that that is -- they have done -- they've used the tools in the same way I have. I disagree with that.
QUESTIONS BY MR. LOCKE:
Q. No, but I'm saying their epidemiology could be the same background that you have. You haven't reviewed who they are, so you really don't really know.
MR. MEADOWS: Objection.
THE WITNESS: Well, I do

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know -- I do know Dr. Klaassen, who I believe was on the panel as a toxicologist. He is not somebody that -- he is not somebody that I understand does a significant amount of evaluation in risk assessment for epidemiological studies. He has done some of that, yes, I agree, but it's different training than mine.
QUESTIONS BY MR. LOCKE:
Q. You're better qualified than he is?
A. No, that's not what I'm saying. I'm saying it's different background.
The question that I heard you ask me, I believe, was directed towards the differences in my background versus somebody else's.
And I'm saying that I'm not aware that he has the same background I do, but there is not -- there was not somebody on the panel that had specific expertise and analysis of epidemiological studies as an epidemiologist. And I think that's important in this case where you're analyzing in a

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causation analysis a wide variety of studies. So I do think it's important.
Q. You're not a gynecological oncologist, are you?
A. No, I'm not. But again, that would have been an important expertise to have on the panel when --
Q. And yet you formed your opinion with --
MR. MEADOWS: Hold on.
MR. LOCKE: No. No. Go ahead. You can ask follow-up questions if you want.
MR. MEADOWS: You're interrupting her.
MR. LOCKE: Well, I've got a limited amount of time, and I've got to keep moving.
MR. MEADOWS: Well --
MR. LOCKE: They're very long answers to questions that I'm not asking. So I -- you follow up if you would like with your questions, but I got to keep moving.
MR. MEADOWS: Well, I'm sorry,

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but you're not going to be allowed to interrupt her.
MR. LOCKE: Okay. Then we'll go longer. If she's going to answer questions I'm not asking, then I need to go -- I need to be able to go longer.
MR. MEADOWS: You're not going to be allowed to interrupt her.
That's just the bottom line.
QUESTIONS BY MR. LOCKE:
Q. You're not a gynecological oncologist, right?
A. I'm not trained as a gynecologic oncologist, that is true.
Q. You're not a medical doctor, correct?
A. I am not a physician, that is correct.
Q. Let's talk about the citizens petition.
The FDA frequently seeks scientific information from cosmetic manufacturers; is that correct?
A. First part of the question?

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I'm sorry.
Q. The FDA frequently seeks information, scientific information, from cosmetic manufacturers; is that correct?
A. I don't understand what you mean by "frequently seeks." They rely on cosmetic manufacturers to do their own safety assessments.
Is that what you're referring to?
Q. Well, they ask PCPC to comment on scientific issues, correct?
A. Yes, I would agree that that interaction has happened, but that's not where the responsibility lies. But I agree, they have.
Q. I'm not asking about responsibility. I'm asking: Has the FDA asked cosmetic manufacturers for scientific information?
A. Yes, they have in this case. I discuss some of that, yes.
Q. And they do that frequently, right? Not just in this case, but generally?
A. I can't answer that for all

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situations. I have seen it happen before, yes.
Q. The FDA asked, for example, for then CTFA to cosponsor the 1994 workshop on talc, correct?
A. Yes, they did.
Q. The FDA knew that the report prepared by Dr. Huncharek and Dr. Muscat was based on PCPC's retention of those consultants, correct?
A. So what are you -- what time period are you talking about?
Q. Well, now, there was only one time that Drs. Huncharek and Muscat submitted a report to the FDA regarding talc, correct?
A. So I need to look to confirm that. Which time period are you talking about?
Q. 2009. Citizens petition.
A. Oh, that is true. In the citizens petition, that is true, yes. But I -- but...
Q. I mean, it says in the letter, "We're submitting a report written by Drs. Huncharek and Muscat," correct?

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A. In the cover letter from the CRE?
Q. From -- not CRE, from PCPC.
A. Okay. So let -- I need to -- I need to refresh my memory on the way the submissions were made. I apologize.
Do you remember which paragraph that you're referring to?
Q. Well, it's throughout your report you're talking about the citizens petition.
A. So it's my recollection, based upon the documents that I have seen, that it was not a transparent process at all times that Drs. Huncharek and Muscat were being identified as independent consultants and were not ones that were being actually paid by the industry for some of the work that they did. And I think that's discussed in my report.
Q. Well, let's break that down.
A. If you want me to confirm the issue of the 2009 -- if you will point me to where you say I discuss this, I will confirm that or not.

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Q. Well, let me break it down.
Citizens petition submitted in 2008, right?
A. Well, there were two: one in 1994 and another -- I'm sorry, 1992, and another in 2008.
Q. Well, there are actually several more than that, but let's just focus on the 2008.
In 2008, a citizens petition was submitted?
A. Yes, that is true.
Q. And PCPC responded to that citizens petition in 2009, correct?
A. They submitted comments. Is that what you're asking me? Yes, they did.
Q. Yes.
And that was a cover letter, correct?
A. A cover letter -- that's all it was was a cover letter?
Q. Well, attached to the cover letter was a report from Drs. Huncharek and Muscat?
A. Yes, that is true.

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Q. And you're not aware of any other document indicating that PCPC ever hired Drs. Huncharek or Muscat?
A. So that's where I'll need to go back and look at the documents, because -- that I have discussed. So I need to find that on my paragraph.
If you want to go off the record for a minute so I don't waste your time, I will look.
Q. Sure.
A. It's up to you. Or we can stay on the record.
MR. LOCKE: I'm fine going off.
VIDEOGRAPHER: We are going off the record at 4:23 p.m.
(Off the record at 4:23 p.m.)
VIDEOGRAPHER: We are back on the record at 4:25 p.m.
QUESTIONS BY MR. LOCKE:
Q. The question I asked: Are you aware of any other document indicating that PCPC ever hired Dr. Huncharek and Muscat other than for the 2009 response or submission to the citizens petition?

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A. I would have to pull this document, but in paragraph 90 I make a statement: A 2005 response written by Dr. Muscat says -- this is not '09, this is 2005, and Dr. Huncharek critiqued the work of Dr. Cramer, who also failed to disclose the financial relation -- I'll start over.
Okay. So I'm sorry to repeat myself, but there was a little noise.
You asked 2009. So the other time period I have in my report in paragraph 90 talks about 2005, but I'd have to pull this document.
But I am citing to the deposition of Dr. Loretz, who was a PCPC employee, so I think I would need to pull this in order to confirm.
But I see depositions of her and Dr. Nicholson as talking about them failing to disclose the financial relationship between their work and industry.
Q. So if Dr. Loretz did not testify that PCPC had retained Drs. Huncharek and Muscat in 2005, you'd have no other evidence?

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A. I can't answer that definitively, but this is what I would point you to. So I'd have to pull these documents to confirm, but I have -- both paragraphs 89 and 90 address these general issues for you, but I think that's the sentence and the documents that I think would be relevant. But I'd have to pull them to fully answer your question.

Q. The reason I ask the question is because you frequently say "the cosmetics industry" without identifying a party or a person. And -- well, I'll just leave it at that.

A. And I guess the reason I'm saying I need to -- I'm questioning that it doesn't have to do with PCPC is because I am citing to a deposition of their employee. So I need to -- I would -- to affirm it, though, I'd need to -- I don't want to say that 100 percent the answer to your question is this is the evidence, but I believe that I would need to go here to confirm one way or the other. But certainly I would -- this raises suspicion about that for me.

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Q. You have no evidence that PCPC ever retained the Center for Regulatory Effectiveness; is that correct?

A. I believe my evidence is hiring through Imerys, but let me look to make sure that is true.

Q. Why don't you look at page -- or I'm sorry, paragraph 95, page 63.

A. That's where I am. That's where I am, so let me read what I have here because it's been a while since I've read this paragraph.

So the question is, do I have in evidence this paragraph that PCPC directly hired the CRE?

No, that is not provided by this paragraph.

Q. Okay.

A. However, in this paragraph, based on these documents that I'm seeing and I'm -- my memory of what is discussed, certainly I believe PCPC would have been aware of the interaction of CRE at these time points when I'm talking about this event -- these events.

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Q. What evidence do you have of that?

A. Based upon the close interaction between PCPC, Imerys and Johnson & Johnson throughout these time periods when different actions were being taken to comment or to submit information on behalf of industry.

Q. Do you have a single document you can point to or is that an assumption?

A. That is something I seem to remember based on my review of these documents, but if you need a document, I would have to -- have to go and look for it.

Q. Sitting here today, you can't recall?

A. I can't give you a specific document as I sit here today, no.

MR. LOCKE: I have no further questions.

MR. MEADOWS: Yeah, short break. Maybe we're done, maybe we're not.

VIDEOGRAPHER: We are going off the record at 4:30 p.m.

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(Off the record at 4:30 p.m.)

VIDEOGRAPHER: We are back on the record at 4:45 p.m.

CROSS-EXAMINATION

QUESTIONS BY MS. PARFITT:

Q. All right. Dr. Plunkett, good afternoon. I know it's been a long day.

Dr. Plunkett, you were asked throughout the course of the day about different constituents which are part of the talcum powder products.

Do you recall those questions?

A. Yes.

Q. All right. If -- without going through each and every one of different constituents that we've talked about that are contained or could be contained in the talcum powder products, if they are present, do those various constituents present and provide biologically plausible evidence that talcum powder products can increase the risk of ovarian cancer?

MS. BOCKUS: Object to the form.

THE WITNESS: Yes, which is --

I think I have a couple of paragraphs where I talk about that issue. It has to do -- there's other information as well, but that is a key piece of that information. And I focused on mode of action and additivity. That's on mechanism, biologic plausibility.

So the fact that you have a variety of constituents that have a known cancer hazard that share a mode of action, that increases your confidence in the biologic plausibility of that relationship between ovarian cancer and exposure to talc body powders, yes.

MS. PARFITT: Thank you. I have no further questions. Thank you very much, Dr. Plunkett. And a happy holiday to you.

THE WITNESS: Thank you.

MS. BRANSCOME: I have no questions.

MS. BOCKUS: No questions.

VIDEOGRAPHER: The time now is 4:47 p.m. This concludes the

deposition, and we are going off the record.

(Deposition concluded at 4:47 p.m.)

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CERTIFICATE

I, CARRIE A. CAMPBELL, Registered Diplomate Reporter, Certified Realtime Reporter and Certified Shorthand Reporter, do hereby certify that prior to the commencement of the examination, Laura Plunkett, Ph.D., DABT was duly sworn by me to testify to the truth, the whole truth and nothing but the truth.

I DO FURTHER CERTIFY that the foregoing is a verbatim transcript of the testimony as taken stenographically by and before me at the time, place and on the date hereinbefore set forth, to the best of my ability.

I DO FURTHER CERTIFY that I am neither a relative nor employee nor attorney nor counsel of any of the parties to this action, and that I am neither a relative nor employee of such attorney or counsel, and that I am not financially interested in the action.

_____

CARRIE A. CAMPBELL,
NCRA Registered Diplomate Reporter
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Notary Public

Dated: 12/20/18

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Please read your deposition over carefully and make any necessary corrections. You should state the reason in the appropriate space on the errata sheet for any corrections that are made.

After doing so, please sign the errata sheet and date it. You are signing same subject to the changes you have noted on the errata sheet, which will be attached to your deposition.

It is imperative that you return the original errata sheet to the deposing attorney within thirty (30) days of receipt of the deposition transcript by you. If you fail to do so, the deposition transcript may be deemed to be accurate and may be used in court.

ACKNOWLEDGMENT OF DEPONENT

I,_____________________, do hereby certify that I have read the foregoing pages and that the same is a correct transcription of the answers given by me to the questions therein propounded, except for the corrections or changes in form or substance, if any, noted in the attached Errata Sheet.

____
Laura Plunkett, Ph.D., DABT DATE

Subscribed and sworn to before me this _______ day of _______________, 20 _____.
My commission expires: _______________

Notary Public

ERRATA

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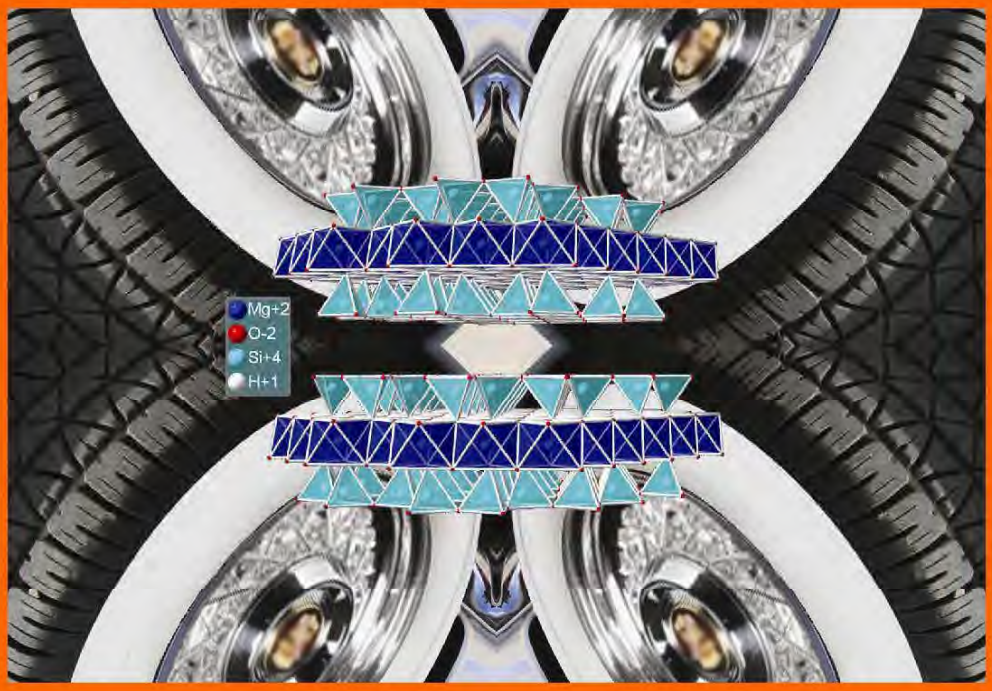
Exhibit V

WORLD HEALTH ORGANIZATION
INTERNATIONAL AGENCY FOR RESEARCH ON CANCER

IARC Monographs on the Evaluation of Carcinogenic Risks to Humans

VOLUME 93

Carbon Black, Titanium Dioxide, and Talc



LYON, FRANCE
2010

WORLD HEALTH ORGANIZATION
INTERNATIONAL AGENCY FOR RESEARCH ON CANCER

IARC Monographs on the Evaluation of Carcinogenic Risks to Humans

VOLUME 93

Carbon Black, Titanium Dioxide, and Talc

This publication represents the views and expert opinions
of an IARC Working Group on the
Evaluation of Carcinogenic Risks to Humans,
which met in Lyon,

7–14 February 2006

2010

IARC MONOGRAPHS

In 1969, the International Agency for Research on Cancer (IARC) initiated a programme on the evaluation of the carcinogenic risk of chemicals to humans involving the production of critically evaluated monographs on individual chemicals. The programme was subsequently expanded to include evaluations of carcinogenic risks associated with exposures to complex mixtures, lifestyle factors and biological and physical agents, as well as those in specific occupations. The objective of the programme is to elaborate and publish in the form of monographs critical reviews of data on carcinogenicity for agents to which humans are known to be exposed and on specific exposure situations; to evaluate these data in terms of human risk with the help of international working groups of experts in chemical carcinogenesis and related fields; and to indicate where additional research efforts are needed. The lists of IARC evaluations are regularly updated and are available on the Internet at http://monographs.iarc.fr/.

This programme has been supported since 1982 by Cooperative Agreement U01 CA33193 with the United States National Cancer Institute, Department of Health and Human Services. Additional support has been provided since 1986 by the Health, Safety and Hygiene at Work Unit of the European Commission Directorate-General for Employment, Social Affairs and Equal Opportunities, and since 1992 by the United States National Institute of Environmental Health Sciences, Department of Health and Human Services. The contents of this volume are solely the responsibility of the Working Group and do not necessarily represent the official views of the U.S. National Cancer Institute, the U.S. National Institute of Environmental Health Sciences, the U.S. Department of Health and Human Services, or the European Commission Directorate-General for Employment, Social Affairs and Equal Opportunities.

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doctoral theses and other material that are in their final form and publicly available may be reviewed.

Exposure data and other information on an agent under consideration are also reviewed. In the sections on chemical and physical properties, on analysis, on production and use and on occurrence, published and unpublished sources of information may be considered.

Inclusion of a study does not imply acceptance of the adequacy of the study design or of the analysis and interpretation of the results, and limitations are clearly outlined in square brackets at the end of each study description (see Part B). The reasons for not giving further consideration to an individual study also are indicated in the square brackets.

5. Meeting participants

Five categories of participant can be present at *Monograph* meetings.

(a) The Working Group is responsible for the critical reviews and evaluations that are developed during the meeting. The tasks of Working Group Members are: (i) to ascertain that all appropriate data have been collected; (ii) to select the data relevant for the evaluation on the basis of scientific merit; (iii) to prepare accurate summaries of the data to enable the reader to follow the reasoning of the Working Group; (iv) to evaluate the results of epidemiological and experimental studies on cancer; (v) to evaluate data relevant to the understanding of mechanisms of carcinogenesis; and (vi) to make an overall evaluation of the carcinogenicity of the exposure to humans. Working Group Members generally have published significant research related to the carcinogenicity of the agents being reviewed, and IARC uses literature searches to identify most experts. Working Group Members are selected on the basis of (a) knowledge and experience and (b) absence of real or apparent conflicts of interests. Consideration is also given to demographic diversity and balance of scientific findings and views.

(b) Invited Specialists are experts who also have critical knowledge and experience but have a real or apparent conflict of interests. These experts are invited when necessary to assist in the Working Group by contributing their unique knowledge and experience during subgroup and plenary discussions. They may also contribute text on non-influential issues in the section on exposure, such as a general description of data on production and use (see Part B, Section 1). Invited Specialists do not serve as meeting chair or subgroup chair, draft text that pertains to the description or interpretation of cancer data, or participate in the evaluations.

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analyses. Irrespective of the source of data for the meta-analyses and pooled analyses, it is important that the same criteria for data quality be applied as those that would be applied to individual studies and to ensure also that sources of heterogeneity between studies be taken into account.

(d) Temporal effects

Detailed analyses of both relative and absolute risks in relation to temporal variables, such as age at first exposure, time since first exposure, duration of exposure, cumulative exposure, peak exposure (when appropriate) and time since cessation of exposure, are reviewed and summarized when available. Analyses of temporal relationships may be useful in making causal inferences. In addition, such analyses may suggest whether a carcinogen acts early or late in the process of carcinogenesis, although, at best, they allow only indirect inferences about mechanisms of carcinogenesis.

(e) Use of biomarkers in epidemiological studies

Biomarkers indicate molecular, cellular or other biological changes and are increasingly used in epidemiological studies for various purposes (IARC, 1991; Vainio *et al.*, 1992; Toniolo *et al.*, 1997; Vineis *et al.*, 1999; Buffler *et al.*, 2004). These may include evidence of exposure, of early effects, of cellular, tissue or organism responses, of individual susceptibility or host responses, and inference of a mechanism (see Part B, Section 4b). This is a rapidly evolving field that encompasses developments in genomics, epigenomics and other emerging technologies.

Molecular epidemiological data that identify associations between genetic polymorphisms and interindividual differences in susceptibility to the agent(s) being evaluated may contribute to the identification of carcinogenic hazards to humans. If the polymorphism has been demonstrated experimentally to modify the functional activity of the gene product in a manner that is consistent with increased susceptibility, these data may be useful in making causal inferences. Similarly, molecular epidemiological studies that measure cell functions, enzymes or metabolites that are thought to be the basis of susceptibility may provide evidence that reinforces biological plausibility. It should be noted, however, that when data on genetic susceptibility originate from multiple comparisons that arise from subgroup analyses, this can generate false-positive results and inconsistencies across studies, and such data therefore require careful evaluation. If the known phenotype of a genetic polymorphism can explain the carcinogenic mechanism of the agent being evaluated, data on this phenotype may be useful in making causal inferences.

(f) Criteria for causality

After the quality of individual epidemiological studies of cancer has been summarized and assessed, a judgement is made concerning the strength of evidence that the agent in question is carcinogenic to humans. In making its judgement, the Working Group

considers several criteria for causality (Hill, 1965). A strong association (e.g. a large relative risk) is more likely to indicate causality than a weak association, although it is recognized that estimates of effect of small magnitude do not imply lack of causality and may be important if the disease or exposure is common. Associations that are replicated in several studies of the same design or that use different epidemiological approaches or under different circumstances of exposure are more likely to represent a causal relationship than isolated observations from single studies. If there are inconsistent results among investigations, possible reasons are sought (such as differences in exposure), and results of studies that are judged to be of high quality are given more weight than those of studies that are judged to be methodologically less sound.

If the risk increases with the exposure, this is considered to be a strong indication of causality, although the absence of a graded response is not necessarily evidence against a causal relationship. The demonstration of a decline in risk after cessation of or reduction in exposure in individuals or in whole populations also supports a causal interpretation of the findings.

A number of scenarios may increase confidence in a causal relationship. On the one hand, an agent may be specific in causing tumours at one site or of one morphological type. On the other, carcinogenicity may be evident through the causation of multiple tumour types. Temporality, precision of estimates of effect, biological plausibility and coherence of the overall database are considered. Data on biomarkers may be employed in an assessment of the biological plausibility of epidemiological observations.

Although rarely available, results from randomized trials that show different rates of cancer among exposed and unexposed individuals provide particularly strong evidence for causality.

When several epidemiological studies show little or no indication of an association between an exposure and cancer, a judgement may be made that, in the aggregate, they show evidence of lack of carcinogenicity. Such a judgement requires firstly that the studies meet, to a sufficient degree, the standards of design and analysis described above. Specifically, the possibility that bias, confounding or misclassification of exposure or outcome could explain the observed results should be considered and excluded with reasonable certainty. In addition, all studies that are judged to be methodologically sound should (a) be consistent with an estimate of effect of unity for any observed level of exposure, (b) when considered together, provide a pooled estimate of relative risk that is at or near to unity, and (c) have a narrow confidence interval, due to sufficient population size. Moreover, no individual study nor the pooled results of all the studies should show any consistent tendency that the relative risk of cancer increases with increasing level of exposure. It is important to note that evidence of lack of carcinogenicity obtained from several epidemiological studies can apply only to the type(s) of cancer studied, to the dose levels reported, and to the intervals between first exposure and disease onset observed in these studies. Experience with human cancer indicates that the period from first exposure to the development of clinical cancer is sometimes longer than 20 years; latent periods substantially shorter than 30 years cannot provide evidence for lack of carcinogenicity.

(d) Mechanistic and other relevant data

Data relevant to the toxicokinetics (absorption, distribution, metabolism, elimination) and the possible mechanism(s) of carcinogenesis (e.g. genetic toxicity, epigenetic effects) are summarized. In addition, information on susceptible individuals, populations and life-stages is summarized. This section also reports on other toxic effects, including reproductive and developmental effects, as well as additional relevant data that are considered to be important.

6. Evaluation and rationale

Evaluations of the strength of the evidence for carcinogenicity arising from human and experimental animal data are made, using standard terms. The strength of the mechanistic evidence is also characterized.

[redacted] recognized that the criteria for these evaluations, described below, cannot encompass all of the factors that may be relevant to an evaluation of carcinogenicity. In considering all of the relevant scientific data, the Working Group may assign the agent to a higher or lower category than a strict interpretation of these criteria would indicate.

These categories refer only to the strength of the evidence that an exposure is carcinogenic and not to the extent of its carcinogenic activity (potency). A classification may change as new information becomes available.

An evaluation of the degree of evidence is limited to the materials tested, as defined physically, chemically or biologically. When the agents evaluated are considered by the Working Group to be sufficiently closely related, they may be grouped together for the purpose of a single evaluation of the degree of evidence.

(a) Carcinogenicity in humans

The evidence relevant to carcinogenicity from studies in humans is classified into one of the following categories:

Sufficient evidence of carcinogenicity: The Working Group considers that a causal relationship has been established between exposure to the agent and human cancer. That is, a positive relationship has been observed between the exposure and cancer in studies in which chance, bias and confounding could be ruled out with reasonable confidence. A statement that there is *sufficient evidence* is followed by a separate sentence that identifies the target organ(s) or tissue(s) where an increased risk of cancer was observed in humans. Identification of a specific target organ or tissue does not preclude the possibility that the agent may cause cancer at other sites.

Limited evidence of carcinogenicity: A positive association has been observed between exposure to the agent and cancer for which a causal interpretation is considered by the Working Group to be credible, but chance, bias or confounding could not be ruled out with reasonable confidence.

Inadequate evidence of carcinogenicity: The available studies are of insufficient quality, consistency or statistical power to permit a conclusion regarding the presence or absence of a causal association between exposure and cancer, or no data on cancer in humans are available.

Evidence suggesting lack of carcinogenicity: There are several adequate studies covering the full range of levels of exposure that humans are known to encounter, which are mutually consistent in not showing a positive association between exposure to the agent and any studied cancer at any observed level of exposure. The results from these studies alone or combined should have narrow confidence intervals with an upper limit close to the null value (e.g. a relative risk of 1.0). Bias and confounding should be ruled out with reasonable confidence, and the studies should have an adequate length of follow-up. A conclusion of *evidence suggesting lack of carcinogenicity* is inevitably limited to the cancer sites, conditions and levels of exposure, and length of observation covered by the available studies. In addition, the possibility of a very small risk at the levels of exposure studied can never be excluded.

In some instances, the above categories may be used to classify the degree of evidence related to carcinogenicity in specific organs or tissues.

When the available epidemiological studies pertain to a mixture, process, occupation or industry, the Working Group seeks to identify the specific agent considered most likely to be responsible for any excess risk. The evaluation is focused as narrowly as the available data on exposure and other aspects permit.

(b) Carcinogenicity in experimental animals

Carcinogenicity in experimental animals can be evaluated using conventional bioassays, bioassays that employ genetically modified animals, and other in-vivo bioassays that focus on one or more of the critical stages of carcinogenesis. In the absence of data from conventional long-term bioassays or from assays with neoplasia as the end-point, consistently positive results in several models that address several stages in the multistage process of carcinogenesis should be considered in evaluating the degree of evidence of carcinogenicity in experimental animals.

The evidence relevant to carcinogenicity in experimental animals is classified into one of the following categories:

Sufficient evidence of carcinogenicity: The Working Group considers that a causal relationship has been established between the agent and an increased incidence of malignant neoplasms or of an appropriate combination of benign and malignant neoplasms in (a) two or more species of animals or (b) two or more independent studies in one species carried out at different times or in different laboratories or under different protocols. An increased incidence of tumours in both sexes of a single

species in a well-conducted study, ideally conducted under Good Laboratory Practices, can also provide *sufficient evidence*.

A single study in one species and sex might be considered to provide *sufficient evidence of carcinogenicity* when malignant neoplasms occur to an unusual degree with regard to incidence, site, type of tumour or age at onset, or when there are strong findings of tumours at multiple sites.

Limited evidence of carcinogenicity: The data suggest a carcinogenic effect but are limited for making a definitive evaluation because, e.g. (a) the evidence of carcinogenicity is restricted to a single experiment; (b) there are unresolved questions regarding the adequacy of the design, conduct or interpretation of the studies; (c) the agent increases the incidence only of benign neoplasms or lesions of uncertain neoplastic potential; or (d) the evidence of carcinogenicity is restricted to studies that demonstrate only promoting activity in a narrow range of tissues or organs.

Inadequate evidence of carcinogenicity: The studies cannot be interpreted as showing either the presence or absence of a carcinogenic effect because of major qualitative or quantitative limitations, or no data on cancer in experimental animals are available.

Evidence suggesting lack of carcinogenicity: Adequate studies involving at least two species are available which show that, within the limits of the tests used, the agent is not carcinogenic. A conclusion of *evidence suggesting lack of carcinogenicity* is inevitably limited to the species, tumour sites, age at exposure, and conditions and levels of exposure studied.

(c) Mechanistic and other relevant data

Mechanistic and other evidence judged to be relevant to an evaluation of carcinogenicity and of sufficient importance to affect the overall evaluation is highlighted. This may include data on preneoplastic lesions, tumour pathology, genetic and related effects, structure–activity relationships, metabolism and toxicokinetics, physicochemical parameters and analogous biological agents.

The strength of the evidence that any carcinogenic effect observed is due to a particular mechanism is evaluated, using terms such as 'weak', 'moderate' or 'strong'. The Working Group then assesses whether that particular mechanism is likely to be operative in humans. The strongest indications that a particular mechanism operates in humans derive from data on humans or biological specimens obtained from exposed humans. The data may be considered to be especially relevant if they show that the agent in question has caused changes in exposed humans that are on the causal pathway to carcinogenesis. Such data may, however, never become available, because it is at least conceivable that certain compounds may be kept from human use solely on the basis of evidence of their toxicity and/or carcinogenicity in experimental systems.

The conclusion that a mechanism operates in experimental animals is strengthened by findings of consistent results in different experimental systems, by the demonstration of

biological plausibility and by coherence of the overall database. Strong support can be obtained from studies that challenge the hypothesized mechanism experimentally, by demonstrating that the suppression of key mechanistic processes leads to the suppression of tumour development. The Working Group considers whether multiple mechanisms might contribute to tumour development, whether different mechanisms might operate in different dose ranges, whether separate mechanisms might operate in humans and experimental animals and whether a unique mechanism might operate in a susceptible group. The possible contribution of alternative mechanisms must be considered before concluding that tumours observed in experimental animals are not relevant to humans. An uneven level of experimental support for different mechanisms may reflect that disproportionate resources have been focused on investigating a favoured mechanism.

For complex exposures, including occupational and industrial exposures, the chemical composition and the potential contribution of carcinogens known to be present are considered by the Working Group in its overall evaluation of human carcinogenicity. The Working Group also determines the extent to which the materials tested in experimental systems are related to those to which humans are exposed.

(d) Overall evaluation

Finally, the body of evidence is considered as a whole, in order to reach an overall evaluation of the carcinogenicity of the agent to humans.

An evaluation may be made for a group of agents that have been evaluated by the Working Group. In addition, when supporting data indicate that other related agents, for which there is no direct evidence of their capacity to induce cancer in humans or in animals, may also be carcinogenic, a statement describing the rationale for this conclusion is added to the evaluation narrative; an additional evaluation may be made for this broader group of agents if the strength of the evidence warrants it.

The agent is described according to the wording of one of the following categories, and the designated group is given. The categorization of an agent is a matter of scientific judgement that reflects the strength of the evidence derived from studies in humans and in experimental animals and from mechanistic and other relevant data.

Group 1: The agent is *carcinogenic to humans*.

This category is used when there is *sufficient evidence of carcinogenicity* in humans. Exceptionally, an agent may be placed in this category when evidence of carcinogenicity in humans is less than *sufficient* but there is *sufficient evidence of carcinogenicity* in experimental animals and strong evidence in exposed humans that the agent acts through a relevant mechanism of carcinogenicity.

Group 2.

This category includes agents for which, at one extreme, the degree of evidence of carcinogenicity in humans is almost *sufficient*, as well as those for which, at the other extreme, there are no human data but for which there is evidence of

carcinogenicity in experimental animals. Agents are assigned to either Group 2A (*probably carcinogenic to humans*) or Group 2B (*possibly carcinogenic to humans*) on the basis of epidemiological and experimental evidence of carcinogenicity and mechanistic and other relevant data. The terms *probably carcinogenic* and *possibly carcinogenic* have no quantitative significance and are used simply as descriptors of different levels of evidence of human carcinogenicity, with *probably carcinogenic* signifying a higher level of evidence than *possibly carcinogenic*.

Group 2A: The agent is *probably carcinogenic to humans.*

This category is used when there is *limited evidence of carcinogenicity* in humans and *sufficient evidence of carcinogenicity* in experimental animals. In some cases, an agent may be classified in this category when there is *inadequate evidence of carcinogenicity* in humans and *sufficient evidence of carcinogenicity* in experimental animals and strong evidence that the carcinogenesis is mediated by a mechanism that also operates in humans. Exceptionally, an agent may be classified in this category solely on the basis of *limited evidence of carcinogenicity* in humans. An agent may be assigned to this category if it clearly belongs, based on mechanistic considerations, to a class of agents for which one or more members have been classified in Group 1 or Group 2A.

Group 2B: The agent is *possibly carcinogenic to humans.*

This category is used for agents for which there is *limited evidence of carcinogenicity* in humans and less than *sufficient evidence of carcinogenicity* in experimental animals. It may also be used when there is *inadequate evidence of carcinogenicity* in humans but there is *sufficient evidence of carcinogenicity* in experimental animals. In some instances, an agent for which there is *inadequate evidence of carcinogenicity* in humans and less than *sufficient evidence of carcinogenicity* in experimental animals together with supporting evidence from mechanistic and other relevant data may be placed in this group. An agent may be classified in this category solely on the basis of strong evidence from mechanistic and other relevant data.

Group 3: The agent is *not classifiable as to its carcinogenicity to humans.*

This category is used most commonly for agents for which the evidence of carcinogenicity is *inadequate* in humans and *inadequate* or *limited* in experimental animals.

Exceptionally, agents for which the evidence of carcinogenicity is *inadequate* in humans but *sufficient* in experimental animals may be placed in this category when there is strong evidence that the mechanism of carcinogenicity in experimental animals does not operate in humans.

Agents that do not fall into any other group are also placed in this category.

5. Summary of Data Reported

5.1 Exposure data

The term 'talc' refers to both mineral talc and industrial mineral products that contain mineral talc in proportions that range from about 35% to almost 100% and are marketed under the name talc. Mineral talc occurs naturally in many regions of the world where metamorphosed mafic and ultramafic rocks or magnesium carbonates occur. Mineral talc is usually platy but may also occur as asbestiform fibres. (Asbestiform refers to a habit (pattern) of mineral growth and not to the presence of other minerals. Asbestiform talc must not be confused with talc that contains asbestos.) Together with platy talc, asbestiform talc is found in the Gouverneur District of New York State, USA, and occasionally elsewhere; it may be associated with other minerals as observed by transmission electron microscopy.

Talc products vary in their particle size, associated minerals and talc content depending on their source and application. Minerals commonly found in talc products include chlorite and carbonate. Less commonly, talc products contain tremolite, anthophyllite and serpentine.

Mineral talc is valued for its softness, platyness, inertness and ability to absorb organic matter. It is used in agricultural products, ceramics, paint and other coatings, paper, plastics, roofing, rubber, cosmetics and pharmaceuticals and for waste treatment. Cosmetic talc, which contains more than 90% mineral talc, is present in many cosmetic products and is used for many purposes, including baby powders and feminine hygiene products. The type of talc that is currently used for cosmetic purposes in the USA does not contain detectable levels of amphibole, including asbestos. It is not known whether this is true in other countries.

Workers are exposed to talc during its mining and milling. Reported geometric mean exposure levels to respirable dust are typically in the range of 1–5 mg/m^3. Workers may also be exposed in user industries, primarily in the rubber, pulp and paper and ceramics industries. Due to the presence of other particulates, exposure levels may be difficult to measure accurately. Consumer exposure by inhalation could occur during the use of loose powders that contain talc.

Accurate estimates of prevalence are not available. However, in some series of controls from epidemiological studies of ovarian cancer, the prevalence of use for feminine hygiene of body powders, baby powders, talcum powders and deodorizing powders, most of which contain cosmetic talc in varying amounts, has been reported to be as high as 50% in some countries. Perineal use for such purposes seems to have been a common practice in Australia, Canada, the United Kingdom, the USA and other countries, including Pakistan. Use of cosmetic talc in the USA has declined steadily since the late 1970s.

5.2 Human carcinogenicity data

The carcinogenic effect of exposure to talc not contaminated by asbestos fibres has been investigated in five independent but relatively small cohort studies of talc miners and millers in Austria, France, Italy, Norway and the USA. The miners and to a lesser extent the millers in these cohorts were also exposed to quartz. In a case–control study nested in the combined cohorts of talc workers from Austria and France, there was no tendency of higher risks for lung cancer by increasing cumulative exposure of workers to talc dust. In four of five studies, it was explicitly stated that no case of mesothelioma was observed. In the two studies from Italy and Norway, which included an estimate of cumulative exposure of the cohort to talc dust, the risk for lung cancer in the highest category was found to be close to or below unity. In the subgroup of miners in the study in the USA, an excess risk for lung cancer was found, which may be have been due to exposure in the workplace to radon daughters and quartz. In all the other groups of workers studied, there was no increased risk for lung cancer.

Female workers in the Norwegian pulp and paper industry had an increased risk for ovarian cancer, which, however, was attributed to exposure to asbestos. A community-based case–control study did not find an increased risk for ovarian cancer associated with occupational exposure to talc, but the prevalence of exposure was low.

Body powder containing talc has been used by women on the perineum (or genital area), on sanitary napkins and on diaphragms. In total, data from one prospective cohort study and 19 case control studies were reviewed in the evaluation of the association of cosmetic talc use and the risk for ovarian cancer. The information collected on perineal talc use varied substantially by study (e.g. ever use versus regular use, and whether information on the mode of application, frequency or duration of use was available).

The cohort study was conducted among nurses in the USA and included 307 cases of ovarian cancer that occurred over 900 000 person years of observation and a maximum of 14 years of follow-up. Information was collected on the frequency but not duration of regular use. Perineal use of talc was not associated with a risk for ovarian cancer.

The 20 case control studies were conducted in Australia, Canada, China, Greece, Israel, Norway, the United Kingdom and the USA (nested case control study), and included between 77 and 824 cases and 46 and 1367 controls. Five were hospital-based designs and the others were population-based studies. The Working Group designated a subset of these studies as being more informative based on the following characteristics: the study was population-based, was of a reasonable size, had acceptable participation rates and included information to allow control for potentially important confounders.

Eight population-based case control studies from Australia, Canada (Ontario) and the USA (two non-overlapping studies in Boston, MA, and one each in California, Delaware Valley, eastern Massachusetts and New Hampshire and Washington State) were thereby identified as being more informative. The selected studies included at least 188 cases and had participation rates that generally ranged from 60 to 75%. Among these eight studies, the prevalence of use of body powder among controls ranged from 16 to 52%; however,

information on exposure was not collected in a comparable manner across studies. In addition, the frequency and duration of use or total lifetime applications were investigated in several studies as well as consideration of prior tubal ligation or simple hysterectomy. Only sparse data were available on whether women had used body powder before or after the mid-1970s.

The relative risks for ovarian cancer among users of body powder (versus non-users) were homogenous across this relatively diverse set of eight studies, each of which indicated a 30–60% increase in risk. Among the other 11 case–control studies, most also reported relative risks of this magnitude or higher. The subset of studies that assessed use of talc on a diaphragm were relatively uninformative due to their lack of precision.

Results on exposure–response relationships were presented in the cohort study and in seven of the more informative case–control studies. In the cohort study, no exposure–response trend was apparent. Positive exposure–response trends were apparent in the two Boston-based studies that presented the most comprehensive analysis. In the Canadian and Californian studies, a non-significant, weakly positive trend was observed for either duration or frequency of use, but not for both. In the other three case–control studies, no consistent trend was observed and the strongest associations tended to be seen among the shorter-term or less frequent talc users.

The cohort study and four of the eight more informative case–control studies presented results on histological type of ovarian cancer. When the analysis of the cohort study was restricted to the 160 serous invasive cases, a statistically significant increase in risk of about 40% was observed. The risk increased with increasing frequency of body powder use. Risks for serous ovarian cancer were somewhat greater than those for other histological types in two of the four case–control studies in which the contrast was reported. Results for other histological types were inconclusive.

The Working Group carefully weighed the various limitations and biases that could have influenced these findings. Non-differential misclassification of talc use, given the relatively crude definitions available, would have attenuated any true association. Although the available information on potential confounders varied by study, most investigators accounted for age, oral contraceptive use and parity. In most studies, only the adjusted relative risks were presented; however, in the three studies in which both age-adjusted and fully adjusted estimates were provided, relative risks did not differ materially, suggesting minimal residual confounding.

It is possible that confounding by unrecognized risk factors may have distorted the results. One or more such factors, if they are causes of ovarian cancer and also associated in the population with perineal use of talc, could induce the appearance of an association between the use of talc and ovarian cancer where there is none. In order for such an unrecognized risk factor to induce the consistent pattern of excess risks in all of the case–control studies, it would be necessary for the factor to be associated with perineal talc use across different countries and different decades. While the range of countries and decades covered by the more informative case–control studies is not very broad, it provides some

diversity of social and cultural context and thereby reduces the likelihood of a hidden confounder.

There was a distinct pattern of excess risk discernible in all of the case–control studies when users were compared with non-users; however, methodological factors needed to be considered. First, while chance cannot be ruled out as an explanation, it seemed very unlikely to be responsible for the consistent pattern of excess risks. A second possible explanation would be recall bias, to which case–control studies may be particularly susceptible. This may have been the case if there had been widespread publicity about the possible association between the use of body powder and cancer. In such circumstances, it is possible that women who had ovarian cancer could be more likely than women who did not to remember or over-report a habit, such as body powder use, if they thought that it may have played a role in their illness..There was a flurry of publicity in the USA in the mid-1970s concerning the possible risks for cancer posed by the use of talc-based body powders. Following an industry decision to market talc powders with no asbestos, it was the opinion of the Working Group that there had not been widespread public concern about this issue, at least until very recently. Therefore, the Working Group considered it unlikely that such a bias could explain the set of consistent findings that stretch over two decades. The Working Group believed that recall bias was a possibility inherent in the case–control studies and could not be ruled out. The Working Group also considered publication and selection biases and these were not judged to have substantially influenced the pattern of findings.

The Working Group searched for documentation on the presence of known hazardous minerals in talc-based body powders. There were strong indications that these products contained quartz in the mid-1970s and still do. There were also indications that occasional small concentrations of asbestos were present in these products before the mid-1970s, but the available information was sparse, sampling methods and detection limits were not described, and the range of locations where data were available was extremely limited. As a result, the Working Group found it difficult to identify a date before which talc-based body powders contained other hazardous minerals and after which they did not, or to have confidence that this would be applicable worldwide. In addition, the epidemiological studies generally do not provide information about the years during which the female subjects were exposed. Consequently, the Working Group could not identify studies in which an uncontaminated form of talc was the only one used by study subjects. Nevertheless, the Working Group noted that, even in the most recent studies in the USA, where exposure histories may have been much less affected by hazardous contaminants of talc, the risk estimates were not different from the early studies in which the possibility of such exposure was more likely.

To evaluate the evidence on whether perineal use of talc causes an increased risk for ovarian cancer, the Working Group noted the following:

- The eight more informative case–control studies, as well as most of the less informative ones, provided overall estimates of excess risk that were remarkably consistent; seven of these eight case–control studies examined exposure–response

relationships; two provided evidence supporting such a relationship, two provided mixed evidence and three did not support an association.

- The cohort study neither supports nor strongly refutes the evidence from the case–control studies.
- Case–control studies were susceptible to recall bias which could tend to inflate risk estimates but to an unknown degree.
- All of the studies were susceptible to other potential biases which could either increase or decrease the association.
- All of the studies involved some degree of non-differential misclassification of exposure that would tend to underestimate any true underlying association.

5.3 Animal carcinogenicity data

Talc of different grades was tested for carcinogenicity in mice by inhalation exposure, intrathoracic, intraperitoneal and subcutaneous injection, in rats by inhalation exposure, intrathoracic injection, intraperitoneal injection, oral administration and intrapleural and ovarian implantation, and in hamsters by inhalation exposure and intratracheal injection.

In male and female rats exposed by inhalation to a well-defined talc, the incidence of alveolar/bronchiolar carcinoma or adenoma and carcinoma (combined) was significantly increased in female rats. The incidence of adrenal medulla pheochromocytomas (benign, malignant or complex (combined)) showed a significant positive trend and the incidence in high-dose males and females was significantly greater than that in controls. The incidence of malignant pheochromocytomas was also increased in high-dose females. The Working Group did not consider it probable that the increased incidence of pheochromocytomas was causally related to talc but, based on the experimental data available, neither could talc-related effects be excluded.

Tumour incidence was not increased following the intrapleural or intrathoracic administration of a single dose of various talcs to rats. In two studies of intraperitoneal administration in rats, no increase in the incidence of mesotheliomas was observed. No increased incidence of tumours was produced in rats in two studies of talc administered in the diet or in another study of the implantation of talc on to the ovary.

Tumour incidence was not increased in mice following the inhalation of talc in one study, the intrathoracic administration of a single dose of various talcs in another study or the administration of talc by intraperitoneal injections in three studies. A single subcutaneous injection of talc into mice did not produce local tumours.

Tumour incidence was not increased following inhalation or intratracheal administration of talc to hamsters.

5.4 Mechanistic considerations and other relevant data

Different mechanisms are probably operative in the effects of talc on the lung and pleura, depending on the route of exposure.

In humans, deposition, retention and clearance of talc have been insufficiently studied, although talc particles have been found at autopsy in the lungs of talc workers.

In humans and experimental animals, the effects of talc are dependent on the route of exposure, and the dose and properties of the talc. Talc pneumoconiosis was somewhat more prevalent and severe among miners exposed to talc containing asbestiform minerals and/or asbestos than among those exposed to talc without such contaminants. However, the role of quartz and asbestos in the observed pneumoconiosis could not be ruled out. Among drug users, intravenous injection of talc present as a filler in the drugs resulted in microembolization in a variety of organs and alterations in pulmonary function.

In animal studies, talc has been shown to cause granulomas and mild inflammation when inhaled. Observations of the effects that occurred in the lungs of rats exposed by inhalation to talc suggested that the operative mechanisms may be similar to those identified for carbon black, and talc is known to cause the release of cytokines, chemokines and growth factors from pleural mesothelial cells.

In humans, intrapleural administration of talc as a therapeutic procedure results in pleural inflammation which leads to pleural fibrosis and symphysis. Pleural fibrosis is the intended effect of intrapleural administration of talc in patients with malignant pleural effusions or pneumothorax. Animal studies suggested that extrapulmonary transport of talc following pleurodesis increases with decreasing particle size and increasing administered dose. Talc has been shown to cause apoptosis of malignant cells *in vitro*.

Perineal exposure to cosmetic talc in women is of concern because of its possible association with ovarian cancer. Several studies have been conducted in women to assess potential retrograde movement of particles through the reproductive tract to the ovaries. These have been conducted in women who were about to undergo gynaecological surgery, most of whom had diseases or complications of the reproductive tract and organs that required surgery. The findings reported in these studies may be confounded by the various levels of dysfunction in clearance from the female reproductive tract due to underlying pathologies. In addition, most of the studies had little or no further information on the use of talc products for perineal hygiene or changes in habits that may have preceded surgery. On balance, the Working Group believed that the evidence for retrograde transport of talc to the ovaries in normal women is weak. In women with impaired clearance function, some evidence of retrograde transport was found. Studies in animals (rodents, langomorphs and non-human primates) showed no evidence of retrograde transport of talc to the ovaries.

In one study, predictors of the presence of antibodies to mucin protein were inversely related to the risk for ovarian cancer and exposure to powder containing talc.

No data were available on the genotoxic effects of exposure to talc in humans. The limited number of studies available on the genetic toxicology of talc *in vitro* gave negative results.

6. Evaluation and Rationale

Cancer in humans

There is *inadequate evidence* in humans for the carcinogenicity of inhaled talc not containing asbestos or asbestiform fibres.

There is *limited evidence* in humans for the carcinogenicity of perineal use of talc-based body powder.

Cancer in experimental animals

There is *limited evidence* in experimental animals for the carcinogenicity of talc not containing asbestos or asbestiform fibres.

Overall evaluation

Perineal use of talc-based body powder is *possibly carcinogenic to humans (Group 2B)*.

Inhaled talc not containing asbestos or asbestiform fibres is *not classifiable as to its carcinogenicity (Group 3)*.

Rationale

In making this evaluation the Working Group considered the human and animal evidence as well as evidence regarding the potential mechanisms through which talc might cause cancer in humans.

The Working Group found little or inconsistent evidence of an increased risk for cancer in the studies of workers occupationally exposed to talc. The studies of talc miners and millers were considered to provide the best source of evidence, but no consistent pattern was seen. One study observed an excess risk for lung cancer among miners, but confounding from exposure to other carcinogens made it difficult to attribute this to talc and no excess risk was seen in millers. Other studies also found no increased cancer risk or no higher risk with increasing cumulative exposure. Overall, these results led the Working Group to conclude that there was *inadequate evidence* from epidemiological studies to assess whether inhaled talc not containing asbestos or asbestiform fibres causes cancer in humans.

For perineal use of talc-based body powder, many case–control studies of ovarian cancer found a modest, but unusually consistent, excess in risk, although the impact of bias and potential confounding could not be ruled out. In addition, the evidence regarding exposure–response was inconsistent and the one cohort study did not provide support for an association between talc use and ovarian cancer. Concern was also expressed that

exposure was defined in a variety of ways and that some substances called talc may have contained quartz and other potentially carcinogenic materials. A small number of Working Group members considered the evidence to be inadequate. Despite these reservations, the Working Group concluded that the epidemiological studies taken together provide *limited evidence* of an association between perineal use of talc-based body powder and an increased risk for ovarian cancer.

In one study of rats that inhaled talc, an excess incidence of malignant lung tumours was seen in females. The same study observed an excess incidence of pheochromocytomas in the adrenal medulla in both sexes, but the Working Group was divided as to whether these rare tumours could be attributed to exposure to talc. Other studies in rats and mice using different routes of administration did not find an excess of cancer, and two studies in rats were considered to be inadequate for evaluation. Based on the one positive study, the Working Group found that there was *limited evidence* of carcinogenicity of inhaled talc in experimental animals. There was no agreement within the Working Group as to whether the evidence on pheochromocytomas should be taken into account in the evaluation of animal data.

Exhibit W

Synergism *see* Chemical Interactions

Synthetic Vitreous Fibers

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- Name: Synthetic vitreous fibers
- Chemical Abstracts Service Registry Number: N/A
- Synonyms: Man-made vitreous fibers, Mineral wool, Glass fibers/wool, Refractory ceramic fibers (RCF)
- Molecular Formula: Varies
- Chemical Structure: Varies

Background

Synthetic vitreous fibers (SVFs) are inorganic fibrous materials made from a broad variety of inorganic substances with an amorphous (vitreous, i.e., noncrystalline) molecular structure. SVFs are manufactured by multiple processes involving the cooling of high-temperature inorganic oxide streams. SVFs have been arbitrarily divided into three general categories based on their composition and application: fiberglass, mineral wools, and refractory ceramic fibers (RCF); however, the recent development of 'hybrid' SVFs has made these classifications obsolete for hazard classification. The fiberglass category includes continuous glass fibers (textile fibers) and glass wools. Fiberglass products are manufactured from powdered sand and consist of silicon and aluminum oxides. The mineral wool category includes rock and slag wools. Similar to fiberglass, mineral wools are primary aluminum and silicon oxides. Rock wool is manufactured from igneous rocks, while slag wool is manufactured from slag from blast furnace steel. Refractory ceramic fibers are specialized fibers that contain a significantly higher amount of alumina than other fibers. Although RCFs are amorphous at low temperatures, they partially crystallize at higher temperatures.

SVF materials can release airborne fibers, some respirable to the lower lung, during manufacturing and installation, and many people have been occupationally exposed since the first development of SVFs in the late nineteenth century. The discovery of potential respiratory health effects of chronic asbestos exposure in the early twentieth century led to concern regarding the potential adverse health effects of chronic inhalation of SVFs. Epidemiological evidence from the post-World War II era suggested that chronic inhalation of asbestos is associated with an elevated risk of thoracic cancers, especially in asbestos workers who smoked cigarettes. In North American asbestos workers, the incidence of death from lung cancer was 4.6 times greater than the incidence among American males. An association between mesothelioma (cancer of the membranes covering the lungs (pleura), other viscera, and lining body cavities) and occupational exposure to asbestos was suggested and eventually confirmed in asbestos miners in South Africa and in retired asbestos workers.

The asbestos saga taught two important lessons: the biological effects of chronic inhalation of any dust must be examined, and the adverse effects of chronic exposure to a dust may be greatly delayed and become apparent only after studying the pulmonary health of a large population of exposed individuals. Thus, much research since has been directed toward determining what types of particles are potentially toxic and why. In the last two decades, much has been learned about the inhalation effects of SVFs. Findings have impacted the development of occupational exposure regulations and carcinogenicity classification systems for SVFs throughout the world.

Uses

SVFs have been used for thermal and acoustical insulation, liquid and gas filtration, industrial textiles, and reinforcement of other materials. Glass, rock, and slag wools are primarily used in insulating materials for homes, building, and appliances. Filament fibers have been used in plastics, cement, papers, roofing materials, and industrial fabrics, as well as for electrical purposes. Special-purpose fibers include glass fibers produced by flame attenuation for special applications such as fluid and air filtration. Electrical glass (E-glass) is a special-purpose fiberglass developed for electrical applications that has heat and water resistance. RCFs are used in insulation that requires very high temperature resistance, such as furnace insulation. The production and use of SVFs have increased over the years, as they are commonly used to replace asbestos.

Environmental Fate and Behavior

SVFs are highly persistent in the environment. While SVFs dissolve readily in aqueous solutions at certain pHs, this is more relevant to biological systems. Transportation of SVFs in the environment is governed by fiber size, and the subsequent ability to remain suspended in ambient air for extended periods of time. As such, inhalation exposure to airborne SVF is the primary health concern for environmental and occupational exposure.

Toxicokinetics

SVFs act through direct contact with lung tissue or by stimulating acute and/or chronic inflammatory responses in lung tissue. This can occur directly through generation of reactive

 http://dx.doi.org/10.1016/B978-0-12-386454-3.01172-6

oxygen species (ROS), or indirectly through macrophage-mediated clearance. Important determinants of SVF toxicity are fiber size, biopersistence, and dose.

The aerodynamic diameter of an SVF determines whether it can be inhaled into the lower lung and where in the lung it will deposit. The actual diameter is much more important than length in determining the aerodynamic diameter, and relatively long fibers with very small diameters can travel with the inhaled air stream deep into the lung. Asbestos fibers as long as 200 μm have been observed in human and rat lung tissue and 40–80% of fibers with aerodynamic diameters <1 μm that are inhaled into the human lower lung travel back out with exhaled air. Lung deposition of SVFs in rats was greatest for fibers with an aerodynamic diameter of 2 μm and most efficient in rats and humans when fiber diameter was less than 3 μm. Inhaled particles with an aerodynamic diameter >3–4 μm tend to deposit in the upper airways and are quickly cleared to the throat by the mucociliary escalator.

While fiber diameter is a major determinant of respirability and lung deposition, fiber length affects the rate of clearance from the lower lung. In the healthy lung, if the exposure is not extreme, small non-fibrous particles and fibers shorter than 15–20 μm are presumably phagocytized and transported quickly by alveolar macrophages (AMs) to the mucociliary escalator and cleared to the throat (exceptions include lung overload, and chemically cytotoxic particles such as crystalline silica). However, fibers longer than 15–20 μm may be too long for AMs to phagocytize and transport, thus clearance of long fibers from the lower lung cannot occur until they dissolve or break transversely into fragments that are short enough to be removed. If fibers are thin, they will gain entry to the deep lung. If they are long and chemically durable, they will accumulate during chronic exposure and will remain in the lung for extended periods of time or, in the case of the very durable amphibole asbestos types (e.g., crocidolite and amosite), indefinitely. The more biopersistent the fiber, the greater its potential to exert biological effects on the lung. Biopersistent fibers may be more likely than biosoluble fibers to be taken up by the lung epithelium and translocated into the interstitium and to the pleural space, where they would continue to cause inflammation. Thus, the more biopersistent fibers have the potential to impact a broader range of target tissues.

Mechanisms of Toxicity

When large numbers of foreign particles of any composition deposit in the airways or bronchiole–alveolar region of the lung, the initial response is irritation followed by inflammation, in which AMs play a central role. The AMs migrate to sites of dust deposition and attempt to phagocytize the particles, destroy them, or translocate them to the mucociliary escalator. Simultaneously, the phagocytes release a complex series of chemical messengers that activate and attract inflammatory cells, stimulating mucus secretion, the generation of reactive oxygen species (ROS), and release of inflammatory mediators. The cascade continues as long as the irritant particles persist, subsiding only when and if the particles are cleared from the lung.

The mechanisms of fiber-induced biological effects are believed to include the following: long, thin fibers are inhaled into the deep lung; durable, long fibers resist lung clearance and degradation; fibers are translocated into the lung interstitium and pleura fibers stimulate the cellular release of inflammatory mediators; chronic release of mediators causes tissue injury, followed by tissue repair and cell proliferation; chronic injury-repair results in fibrosis; and advancing fibrosis and chronic proliferation may contribute to carcinogenesis. Additionally, fibers may directly physically or chemically (e.g., by free radicals) induce neoplastic changes in the genetic material of the cell or act as cocarcinogens or promoters in concert with other substances such as tobacco smoke.

All of these factors are affected by the target-organ (lung) dose over time, which is determined by lung deposition (respirability) and retention of fibers. Deposition and retention are determined by fiber size and shape, and retention is additionally determined by physical and chemical durability. Fiber surface reactivity, especially in regard to the ability to generate ROS, may play a role in toxicity and genotoxicity. Impacting the potential pathogenesis are other factors that compromise pulmonary health, including previous or current disease and exposure to toxic cofactors such as cigarette smoke, dusts, vapors, or fumes.

Acute and Short-Term Toxicity

Studies examining acute toxicity of SVF exposure are limited. Most studies examine the longer term effects (lung cancer, mesothelioma) of a single or occupational exposure to SVFs, indicating that acute toxic responses are not significant. Acute exposure in animal studies caused pulmonary and pleural inflammation directly related to fiber size and exposure dose. In general, SVF exposure induces eye and upper respiratory tract irritation as well as dermal irritation often classified as 'fiberglass itch.' Respiratory tract irritation may present as sore throat, nasal congestion, laryngeal pain, and cough. These symptoms do not persist postexposure.

Chronic Toxicity

Mortality Studies: Fiberglass and Mineral Wool (Occupational Exposure)

Two major mortality studies have been conducted on fiberglass and mineral wool manufacturing workers in Europe and the United States, while a smaller study was conducted in Canada. The European study followed the mortality of 25 000 manufacturing workers in SVF factories through 1977, with a follow-up through 1982, and a final update through 1990 for most plants. The glass wool subcohort showed no elevation in mortality due to lung cancer when compared with local mortality rates, and the continuous glass filament subcohort did not show any significant elevations in mortality. The rock wool/slag wool subcohort showed an excess of lung cancer mortality (using both national and local mortality rates). However, the researchers concluded that the mesothelioma mortality incidence in the rock/slag wool subcohort (0.03%) 'may not

represent an excess.' Both the original study and the updated studies found no association between employment in fiberglass or mineral wool manufacturing and increased mortality from other cancers, or from nonmalignant respiratory diseases.

US researchers conducted a comprehensive review of 16 646 workers at fiberglass and mineral wool manufacturing plants, many of who had long-term occupational SVF exposure. The study indicated some small but statistically significant excesses in lung cancer mortality among the fiber workers. The respiratory cancer standard mortality ratio was higher among mineral wool workers than among glass wool and glass textile workers. However, the data were not consistent with a causal relationship, because there was no pattern of increased risk related to duration of employment or individual worker exposure. A recent update confirmed previous findings, and with additional information regarding employee smoking habits, established no significant association between fiber exposure and the earlier observed increase in respiratory disease. The study determined that the excess of lung cancer mortalities was due to smoking habits and not SVF exposure. A case–control study of mortality among employees in slag wool manufacturing plants also found no increased risk of lung cancer associated with exposure to slag wool, but did observe increased risk with increasing pack-years of cigarette smoking.

Another study examining 2557 male workers at a glass wool manufacturing plant reported a statistically significant excess in lung cancer mortality among the fiberglass workers. They concluded that the interpretation of this finding was difficult because there was no relationship between lung cancer and length of time since first exposure to the fiberglass production environment. Epidemiologists at Harvard University reviewed the various studies of fiberglass and mineral wool workers and made similar conclusions.

Morbidity Studies: Fiberglass and Mineral Wool

A morbidity study on the respiratory health of 1089 workers employed at fiberglass and mineral wool plants found the employees to be generally healthy, with no respiratory symptoms or adverse lung functions related to fiber exposure. The study was later enlarged to include over 1435 workers and included over 300 local comparison workers (who had not worked with fibers). Looking at the follow-up study as a whole, the results showed no signs of health effects due to SVF exposure in the workers.

Morbidity Studies: Refractory Ceramic Fiber

As a product manufactured for a specific niche, the estimated exposed population involved in the manufacture, distribution, installation, conversion, and end use of RCF is small. Studies showed that lung function among RCF workers was significantly reduced among males who were current or past cigarette smokers, but not among those who had never smoked. In contrast, female lung function was significantly reduced for nonsmokers but not smokers. However, the employment periods for the women were mostly quite short, and the numbers in the female subcohorts were small, especially when divided into smokers and never-smokers. A follow-up longitudinal study of a subgroup of the male employees found no additional yearly loss in lung function among the RCF employees, probably due to lower RCF exposure in the manufacturing plants since the 1980s. Similar results were reported in a group of European RCF manufacturing workers, though the researchers concluded that cumulative exposure to RCFs may have caused airway obstruction by promoting the effects of cigarette smoke.

Chronic Inhalation Studies in Animals

Several chronic, multi-dose studies have been performed in rodents, examining the carcinogenicity potential of various SVFs, especially in regard to lung cancer and mesothelioma. Early studies in rats exposed to two types of building insulation fiberglass: JM901 and CertainTeed, showed that they induced only transient lung inflammation that disappeared after a post-exposure recovery period. None of the exposed rats developed fibrosis, and lung tumor incidence was at background levels. Conversely, very high exposure to chrysotile asbestos and crocidolite asbestos induced lung fibrosis and pulmonary tumors. Tumor incidences were 20% for chrysotile (13 lung tumors and 1 mesothelioma) and 14% for crocidolite (15 lung tumors and 1 mesothelioma). Hamsters exposed to JM901 also did not develop fibrosis or thoracic neoplasms.

Although very high exposures to chrysotile asbestos ($\sim$1 million f cm^{-3}) resulted in lung fibrosis, lung cancer, and a few mesotheliomas in rat inhalation studies, recent studies indicate that chrysotile is very biosoluble, having half-times of clearance from the lung between 0.3 and 11.4 days (Table 1). Furthermore, a chrysotile exposure level of 536 f cm^{-3} resulted in no lung fibrosis or any other pathological changes in rat

Table 1 Correlation of results from biopersistence and inhalation toxicity

	Biopersistence	*Inhalation toxicity*	
Fiber	*Half-life (days)*	*Fibrosis*	*Tumors*
Crocidolite asbestos	817	+	+
Amosite asbestos	418	+	+
E-glass – special-purpose fiberglass	79	+	+
RCF1 – refractory ceramic fiber	55	+	+
JM475 – special-purpose fiberglass	49	+	–
Rock wool	67	+	–
JM901 – insulation wool fiberglass	37	–	–
JM901.1 – insulation wool fiberglass	14.5	–	–
X607	9.8	–	–
CertainTeed – insulation wool fiberglass	9	–	–
Slag wool	9	–	–
Stone wool	6	–	–
Chrysotile asbestos[a]	0.3–11.4	–	ND

ND, not determined.
[a]While studies have shown that very high exposures to chrysotile asbestos can induce fibrosis and pulmonary tumors, a 90 day inhalation study in rats exposed to 536 f cm^{-3} resulted in no fibrosis. Pulmonary tumors in lower exposures have not been determined.
Adapted from: Hesterberg, T.W., Chase, G., Axten, C., Miller, W.C., Musselman, R.P., Kamstrup, O., Hadley, J., Morscheidt, C., Bernstein, D.M., Thevenaz, P., 1998. Biopersistence of synthetic vitreous fibers and amosite asbestos in the rat lung following inhalation. Toxicol. Appl. Pharmacol. 151(2), 262–275.

lungs after 90 days of inhalation exposure. It has been well documented in the peer-reviewed literature that if fibrosis is not observed after 90 days of inhalation exposure to fibers, then no lung cancer or mesotheliomas will be observed after chronic inhalation to fibers for up to 3 years. Thus, one would predict that chrysotile exposures below 536 f cm^{-3} would not result in lung cancer or mesotheliomas in a rat inhalation study.

In addition to JM901, the hamster chronic inhalation study also tested a relatively durable special application fiberglass, JM475, and amosite asbestos (Table 1). During the first 12 months of exposure, amosite asbestos fibers >20 μm accumulated in the lungs in quantities that suggested little or no clearance, whereas lung burdens of JM475 glass fiber (a durable special-purpose fiberglass) and JM901 glass fiber (an insulation wool fiberglass) plateaued at a level 10–37-fold less than that of amosite, suggesting greater clearance rates for these types of fiberglass. Although hamsters exposed to JM901 developed no permanent pulmonary or thoracic changes during the 18 month exposure and 5 week recovery periods, hamsters exposed to the more durable JM475 glass fibers developed minimal lung fibrosis and one mesothelioma (in 83 animals at risk; 1.2% tumor incidence) (Table 1). Hamsters exposed to amosite asbestos at a comparable aerosol concentration or a comparable lung dose also developed fibrosis, but earlier and more severe than that in the animals exposed to JM475. Hamsters exposed to amosite developed mesotheliomas at all doses.

In recent mineral wool studies, rats were exposed by nose-only inhalation to rock and slag wool in three concentrations for 6 h day^{-1}, 5 days $week^{-1}$, for 24 months. In agreement with the earlier inhalation studies of mineral wool, neither test fiber was tumorigenic. However, the rock wool-exposed rats developed minimal fibrosis. In a later chronic inhalation study also using rats, IIT stone wool, at a concentration similar to those of rock and slag wool, induced only transient lung irritation; no fibrosis was observed and the incidence of thoracic tumors was not elevated over that of air-breathing chamber controls. A fourth fiber that could be considered a hybrid between mineral wool and fiberglass, X607, was also found to be innocuous in a 2 year rat chronic inhalation study, and again demonstrated the relationship between biopersistence and pathogenicity. After chronic exposure, fibers/lung (especially long fibers) were much lower for X607 than for RCF1, demonstrating less biopersistence for X607. Chemical analysis of lung fibers confirmed the lower biopersistence of X607, in that these fibers showed rapid leaching, whereas RCF1 lung fibers did not.

Inhalation studies have also examined the carcinogenic potential of RCFs over chronic exposures. Rats and hamsters were exposed to RCF for 6 h day^{-1} and 5 days $week^{-1}$, at a maximum dose of 30 mg m^{-3} for either 24 months (rats) or 18 months (hamsters). Rats were exposed to one of four different types of RCF (RCF1 (kaolin), RCF2 (zirconium), RCF3 (high purity), and RCF4 (after service)), and hamsters were exposed only to kaolin-based RCF1. Rats exposed to any of the four RCFs developed lung fibrosis, and those exposed to RCF1, 2, or 3 had elevated incidences of lung tumors (9–19%) and mesotheliomas (2–3%). Rats exposed to RCF4 did not develop increased lung tumors (3.4%) but did have one (1.4%) mesothelioma (Table 1). Compared with RCF1, 2, and 3, RCF4 was on average shorter and thicker and resulted in lower lung burdens of fibers >20 μm. Hamsters exposed to RCF1 also developed lung fibrosis, but they developed no lung tumors and a high (41%) incidence of mesotheliomas. These studies demonstrate a striking difference between rat and hamster responses to the same test fiber. After lifetime exposure to RCF1, the tumor incidences in rats vs hamsters were 13 vs 05 for lung cancer and 1.7 vs 41% for mesothelioma, respectively. Such a lack of agreement in response raises questions regarding species-related differences and which species, if either, is representative of humans.

In a subsequent study, rats were exposed to three lower doses of RCF1: 3, 9, and 16 mg m^{-3} or to filtered air. The RCF1-exposed rats at each of these doses showed some minimal, dose-dependent lung fibrosis later in the study. RCF1 at these exposure levels did not significantly elevate lung tumor incidence. The lung tumor incidences in the fiber-exposed groups, while higher than that in the concurrent negative controls (0.8%), were well within the reported background rates of 0–8% for adenoma and 0–6% for carcinoma for F344 rats through 24 months. However, one thoracic mesothelioma was observed in the rats exposed to 9 mg m^{-3}. Considering the two rat studies of RCF1, which together included four dose groups (3, 9, 16, and 30 mg m^{-3}), the authors concluded that the fact that the RCF used in this study did not demonstrate lung carcinogenicity at 3, 9, or 16 mg m^{-3} but did at 30 mg m^{-3} is significant. The lack of carcinogenicity at lower doses implies the existence of a threshold delivered dose, below which tumors will not have time to develop within the animal's life span. However, one must not discount the occurrence of one (0.8%) mesothelioma in the 9 mg m^{-3} group and lung fibrosis in all rats in the 9 and 16 mg m^{-3} groups at 12 months and thereafter. One mesothelioma in the 16 mg m^{-3} group may not be considered statistically significant, but due to its rarity as a spontaneous occurrence in rats, it is biologically significant. Although a cause and effect relationship between the development of fibrosis and the development of tumors has not been established, the two events are closely associated, with a lag time of 9–12 months for the appearance of tumors.

Fiber Biopersistence Studies in Rodents

All of the rodent chronic inhalation studies of vitreous and asbestos fibers indicated a relationship between persistence of fibers in the lung and the severity of their biological effects. The term 'lung biopersistence' was coined to refer to the capacity of fibers to preserve their chemical and physical features over time in the lung. During lung residency, pathogenic fibers such as crocidolite or amosite asbestos demonstrated the following:

- Little or no change in chemical composition or surface morphology (suggesting no significant leaching).
- Little or no decrease in diameter or length (suggesting no significant dissolution or transverse fragmentation).

- More rapid clearance of shorter fibers than of longer fibers (suggesting preferential clearance of short fibers by AMs).

In contrast, nonpathogenic fibers, such as HT Stone wool and fiberglass building insulations, demonstrated the reverse of each of these behaviors over time in the lung:

- Compositions changed and surfaces often showed signs of erosion.
- Average fiber dimensions decreased.
- The number of long fibers/lung decreased more rapidly than the number of short fibers/lung (suggesting transverse fragmentation).

The biopersistence–pathogenicity relationship suggested that biopersistence is a key determinant of pathogenicity and might be used to assess the potential carcinogenicity of inorganic fibers. Changes in fiber numbers, chemistry, dimensions, or morphology during lung residency were more pronounced in the eight SVFs than in the two asbestos types. These changes were especially striking in the biosoluble SVFs that cleared more rapidly in the biopersistent studies and were nonpathogenic in the chronic studies (JM901, CertainTeed, slag wool, and stone wool; Table 1). Fiber toxicity was associated with fiber biopersistence in the lung and to a lesser extent with *in vitro* dissolution rate. These observations support the hypothesis that biopersistence of inorganic fibers in the lung is a strong indicator of potential toxicity and is determined in part by fiber dissolution rate.

A model of fiber degradation involving incongruent dissolution (leaching) and breakage could explain why, in the lung burdens of the less persistent fibers, long fibers tended to decline more rapidly than short fibers. In this model, transverse breakage adds to the number of short fibers while macrophage-mediated clearance subtracts from it. The chemical and morphological changes of the biosoluble SVFs observed in the lung fibers further support a model of leaching and breakage: as the more soluble constituents of the fibers leave the silica matrix, the surface becomes pitted or eroded, the depleted fiber matrix weakens and becomes increasingly susceptible to fragmentation. Thus, the biopersistence of lung fibers appears to be determined by the interactions of a number of parameters, including dissolution and leaching in biological fluids, fragmentation, and macrophage-mediated clearance.

Immunotoxicity

There are currently no studies on the potential immunotoxic effects of SVFs. While studies in inhalation exposure have shown localized immune response induction, this induction ceased upon clearance from the lung, and systemic adverse effects have not been identified.

Reproductive and Development Toxicity

There are currently no studies on the potential reproductive effects of SVFs. As the primary mechanism of exposure is inhalation, and SVFs are not readily absorbed into the body, there is no basis for the evaluation of reproductive toxicity.

Genotoxicity

Several SVFs have been found to not be genotoxic in bacterial mutations assays. However, other *in vitro* experiments have implicated SVFs in chromosomal aberrations, morphological transformations, nuclei variation (micro and multinuclei), polyploidy, and DNA breaks and crosslinks. Several SVF types with certain bioreactivities have been shown to damage DNA through generation of ROS. However, SVFs are often less genotoxic than asbestos fibers, and their potency is mediated by their size. Currently, there are no *in vivo* studies to determine the genotoxicity of SVFs in animals.

Carcinogenicity

Little evidence of adverse health effects has been found in several large, ongoing epidemiology studies of SVF manufacturing workers. There is no consistent evidence of an association between exposure to fiberglass and the development of respiratory disease or lung cancer. Some evidence of increased incidence of respiratory disease has been associated with exposure to mineral wools, which could be a carryover from an earlier time when dust controls were not as well developed as today. Studies of RCF workers found no pulmonary fibrosis or neoplastic disease, an elevated incidence (overall, ~3%) of pleural plaques, and some possible decrements in lung function among workers that smoke or have smoked tobacco products.

Based on the chronic and subchronic studies discussed earlier, RCF and certain special-purpose SVFs are the only SVFs to have shown carcinogenicity in animal studies. As such, the International Agency for Research on Cancer (IARC) has classified RCFs and certain special-purpose SVFs as a possible human carcinogens (Group 2B), while glass wool, stone wool, slag wool, and glass fibers are considered not classifiable as to human carcinogenicity (Group 3). Similarly, the EPA has classified RCFs as a Group B2, probable human carcinogen, but has not classified other SVFs in regards to their carcinogenicity. The American Conference of Governmental Industrial Hygienists (ACGIH) classifies RCF as a probable human carcinogen, with lower classifications (confirmed animal carcinogen and not classifiable) assigned to other types of SVFs.

Clinical Management

No biomarkers of disease induced by SVFs are currently known. The chest X-ray is the most commonly used diagnostic technique for the detection of lung injuries such as neoplasms, pleural plaques, or other significant injury. However, this detection is possible only after significant injury, and is not specific to the detection of SVFs, but rather any lung injury (e.g., cigarette smoking, asbestos, and other lung-related toxicants).

Ecotoxicology

No studies have documented toxicity to nonhuman species due to environmental exposure. Since toxic studies in rodents have established lung responses, it is likely that inhalation exposures to animals and wildlife may induce similar respiratory effects.

Exposure Standards and Guidelines (Table 2)

Table 2 SVF regulatory guidelines

OSHA PEL – TWA	
[a]Mineral fibers are currently only regulated as nuisance dust	
General industry	
Inert or nuisance dust	
Respirable fraction	5 mg m^{-3}
Total dust	15 mg m^{-3}
Shipyard	
Fibrous glass	
Respirable fraction	5 mg m^{-3}
Total dust	15 mg m^{-3}
Shipyard	
Mineral wool	
Respirable dust	5 mg m^{-3}
Total dust	15 mg m^{-3}
ACGIH TLV – TWA	
Synthetic vitreous fibers	
Continuous filament glass fibers[a] (A4)	1 f cm^{-3}
Continuous filament glass fibers[b] (A4)	5 mg m^{-3}
Glass wool fibers[a] (A3)	1 f cm^{-3}
Rock wool fibers[a] (A3)	1 f cm^{-3}
Slag wool fibers[a] (A3)	1 f cm^{-3}
Special-purpose glass fibers[a] (A3)	1 f cm^{-3}
Refractory ceramic fibers[a] (A2)	0.2 f cm^{-3}
NIOSH REL – TWA	
Fibrous glass dust (1977 proposal)	
Total dust	5 mg m^{-3}
Fibers with diameter equal or less than 3.5 μm, and length equal to or greater than 10 μm	3 f cm^{-3}

[a]Fibers longer than 5 μm; diameter less than 3 μm; aspect ratio greater than 5:1.
[b]Inhalable fraction.
A2 – Suspected human carcinogen; A3 – Confirmed animal carcinogen with unknown relevance to humans; A4 – Not classifiable as a human carcinogen.

See also: Asbestos; Respiratory Tract Toxicology.

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Exhibit X

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Fellowship in Molecular Biology, Henry Ford Hospital, Detroit, MI	1988–1990

FACULTY APPOINTMENTS:

Adjunct Associate Professor, Department of Oncology, Karmanos Cancer Institute, Detroit Medical Center/Wayne State University School of Medicine, Detroit, MI	2017–Present
Director, Ovarian Cancer Biology Research, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI	2009–Present
Scientific Member, Karmanos Cancer Institute, Molecular Biology and Genetics Program, Wayne State University School of Medicine, Detroit, MI	2008–Present
Member of Tumor Biology and Microenvironment Program, Karmanos Cancer Institute, Detroit, MI	2007–Present
Associate Professor (secondary), Department of Physiology, Wayne State University School of Medicine, Detroit, MI	2008–Present
Associate Professor (primary), Department of Obstetrics and Gynecology,	2007–Present

Wayne State University School of Medicine, Detroit, MI

Tenure, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI	2007–Present
Associate Status, Department of Anatomy/Cell Biology, Wayne State University School of Medicine, Detroit, MI	2003–Present
Tenure Track, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI	2001–2007
Assistant Professor, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI	1998–2007

HOSPITAL OR OTHER PROFESSIONAL:

Senior Investigator, Center for Biomedical Research, Oakland University, Rochester, MI	1997–1998
Adjunct Associate Professor, Department of Chemistry, Oakland University, Rochester, MI	1996–2004
Bioscientific Staff Investigator, Dermatology Department, Henry Ford Hospital, Detroit, MI	1995–1998
Associate Staff Investigator, Department of Dermatology, Henry Ford Hospital, Detroit, MI	1993–1994
Special Lecturer, Department of Chemistry, Oakland University, Rochester, MI	1991–1996
Assistant Staff Investigator, Hypertension Research, Henry Ford Hospital, Detroit, MI	1990–1992
Technical Manager, Pharmaceutical Company, Riyadh, Saudi Arabia	1987–1988
Research Assistant, Biochemistry Department, King Saud University, Riyadh, Saudi Arabia	1982–1983

MAJOR PROFESSIONAL SOCIETIES

Associate Member, Society for Gynecologic Oncology	2017–Present
Member, American Association of Cancer Research	2008–Present
Member, American Federation of Clinical Research	2009–Present
Member, American Society for Reproductive Medicine	1998–Present
Member, Society for Reproductive Investigation	1998–Present
Member, American Association of University Professors	1996–Present
Member, American Chemical Society	1991–2014
National Research Council of the United Kingdom	1985–1986
Medical Research Council of the United Kingdom	1984–1998

HONORS/AWARDS:

Star Award 2017
73rd American Society for Reproductive Medicine (ASRM) Scientific Congress & Expo
This award recognizes members who have presented during at least nine of the ASRM Annual Meetings from the years 2007-2016. Presentations may include Congress courses and/or seminars, Scientific Program symposia, posters, and/or oral presentation of abstracts. 234 awardees

Award for Research 2017

Awarded to Nicole King, PhD, Postdoctoral Fellow in the laboratory of Dr. Ghassan Saed
73rd American Society for Reproductive Medicine (ASRM Scientific Congress & Expo
The purpose of this award is to recognize outstanding research conducted by individuals in training under the "Reproductive Surgery" category. He/she is a presenting first author, and a medical student, resident, fellow, or under-graduate, graduate, or postdoctoral student. Three awardees

Star Award 2016
72nd American Society for Reproductive Medicine (ASRM) Scientific Congress & Expo
This award recognizes members who have presented during at least nine of the ASRM Annual Meetings from the years 2007-2015. Presentations may include Congress courses and or seminars, Scientific Program symposia, posters, and/or oral presentation of abstracts. ~235 awardees

Excellence in Biomedical Research 2015
Global Medical Discovery Series
Key Scientific Article for peer-reviewed publication entitled: "Sox2 Gene Amplification Significantly Impacts Overall Survival in Serous Epithelial Ovarian Cancer." Reproductive Sciences 22(1):38-46, 2015. Epub July 18, 2014. One awardee

Star Award 2013
69th American Society for Reproductive Medicine Annual Meeting (ASRM)
This award recognizes members who have presented during at least nine of the ASRM Annual Meetings from the years 2007-2012. Presentations may include Congress courses and/or seminars, Scientific Program symposia, posters, and/or oral presentation of abstracts. ~235 awardees

Star Award 2011
67th American Society for Reproductive Medicine (ASRM) Annual Meeting
This award recognizes members who have presented during at least nine Of the ASRM Annual Meetings from the years 2007-2010. Presentations may include Congress courses and/or seminars, Scientific Program symposia, posters, and/or oral presentation of abstracts. ~235 awardees

President's Award for Excellence in Teaching 2009
Wayne State University School of Medicine
This award is in recognition for outstanding faculty who have made contributions to teaching at WSU to an exceptionally high degree, demonstrate comprehensive knowledge of their subject, superior classroom performance, and high educational standards; communicate their subject matter accurately, clearly, and effectively; generate enthusiasm and respect for learning; motivate their students to excel; and are accessible to students; innovative instructional practices, impact on teaching at WSU, and contributions to advancing teaching in their field.

Finalist Paper 2006
62nd American Society for Reproductive Medicine (ASRM) Annual Meeting
One awardee

Prize Paper Candidate 2005
Conjoint 61st American Society for Reproductive Medicine (ASRM) Annual Meeting and 51st Canadian Fertility and Andrology Society Annual Meeting
One awardee

Finalist Paper 2005
61st American Society for Reproductive Medicine (ASRM) Annual Meeting
One awardee

Finalist Paper 2003
Society of Reproductive Endocrinology and Infertility (SREI) Annual Meeting
One awardee

Finalist Paper, Basic Science 2003
19th European Society of Human Reproduction and Embryology (ESHRE) Annual Meeting
One awardee

Award Paper 2000
58th Society of Reproductive Surgeons (SRS) Scientific Program

Finalist Paper 2000
Society of Reproductive Endocrinology and Infertility (SREI) Annual Meeting
One awardee

Award Paper 1998
52nd Society of Reproductive Surgeons (SRS) Scientific Program

Outstanding Professor of the Year Award 1996–1997
Golden Key National Society, Oakland University Chapter, Rochester, MI
One awardee

SERVICE:

Wayne State University

Departmental/Divisional

Chairperson, Organizing Committee, 2017 Joint Annual Reproductive Sciences Retreat, Departments of Obstetrics and Gynecology, Wayne State University School of Medicine and University of Toronto; and The Michigan Alliance for Reproductive Technologies and Sciences (MARTS) Annual Meeting at Wayne State University	2017
Faculty Mentor, NIH/NICHD Women's Reproductive Health Research (WRHR) Scholar Program, Department of Obstetrics and Gynecology	2012–2016
Faculty Associate, Fulbright Visiting Senior Scholar Award recipient Dr. Iyad Ali, Department of Obstetrics and Gynecology	2012–2014
Member, Selective Salary Committee, Department of Obstetrics and Gynecology	2012–Present
Member, Promotion and Tenure Committee, Department of Obstetrics and Gynecology	2012–Present
Chairperson, C.S. Mott Center Seminar Series Committee, Department of Obstetrics and Gynecology	1998–Present
Chairperson, Basic Research Endocrine Fellows Training Committee, Department of Obstetrics and Gynecology	1998–2014
Member, Reproductive Endocrinology and Infertility Fellowship Selection Committee, Department of Obstetrics and Gynecology	1998–Present

School of Medicine

Member, Strategic Research Initiative Grant Review (SRIG) Committee, Karmanos Cancer Institute	2013–2014
Member, PhD Committee for Batoul Abdullah, PhD Candidate, Center for Molecular Medicine and Genetics, Wayne State University	2012–2016
Member, PhD Committee for Jimmy Belotte, MD, PhD Candidate, Department of Physiology and Reproductive Sciences, Department of Obstetrics and Gynecology, Wayne State University	2012–2016
Faculty, Reproductive Sciences Graduate Program, Department of Physiology, Wayne State University	2012–2016
Member, Search Committee for a candidate selection for a joint appointment in Departments of Psychology and Obstetrics & Gynecology in the field of Psychopharmacology	2003–2005

Affiliate Medical Organizations

Member, Karmanos Cancer Institute, Molecular Biology and Genetics Program, Detroit, MI	2008–Present
Member of Tumor Biology and Microenvironment Program, Karmanos Cancer Institute, Detroit, MI	2007–Present

Professional

President, National Arab American Medical Association, Michigan Chapter, Troy, MI	2017–Present
Judge, American Society for Reproductive Medicine (ASRM) Abstract Selection Committee, Birmingham, AL	2015–Present
President, National Arab American Medical Association, Michigan Chapter, Troy, MI	2014–2015
Board Member, National Arab American Medical Association, Michigan Chapter, Troy, MI	2009–Present
Judge, Poster Finals Prize Committee, 2002 Annual Meeting of the American Society for Reproductive Medicine (ASRM), Birmingham, AL	2002–2003

Community

Biohazard and Safety Committee, Henry Ford Hospital, Detroit, MI	1996–1998
Radioisotope Safety Committee, Henry Ford Hospital, Detroit, MI	1996–1998
Journal Club Committee, Department of Dermatology, Henry Ford Hospital, Detroit, MI	1994–1998
Basic Research Training Committee, Department of Dermatology, Henry Ford Hospital, Detroit, MI	1994–1998
Animal Care Committee, Henry Ford Hospital, Detroit, MI	1993–1996

Consulting

Consultant, Molecular Biologic Testing, DS Biotech, Detroit, MI	2013–Present
Consultant, Application of Cyclooxgenase-2 in the Treatment of Ovarian Cancer, Pfizer Pharmaceuticals, Rochester, MI	2002
Consultant, Technical expertise in developing molecular probes and markers, Oxford Biomedical Research, Oxford, MI	1991–1998

Scholarly Service

<u>Grant Review Committees</u>

Member, Scientific Review Committee, Ethel F. Donoghue Women's Health Investigator Program, Yale University, New Haven, CT	2004

Service for Peer-Reviewed Journals Editorship

Editorial Board Membership:

Editor-in-Chief, Gynecology and Obstetrics Research-Open Journal	2015–Present

Review of Manuscripts and Chapters:

Journal of Cellular and Molecular Medicine	2015–Present
Systems Biology in Reproductive Medicine	2013–Present
Journal of Assisted Reproduction and Genetics	2013–Present
Journal of Reproductive Science	2012–Present
European Journal of Obstetrics & Gynecology and Reproductive Biology	2009
Gastroenterology	2007
Houghton Mifflin Company, College Division	2003
American Gynecological and Obstetrical Society	2003
Oncogenes	2003
Fertility and Sterility	2001–Present
Wound Repair and Regeneration	2000–Present
Journal of Cytokine Research	1998–2000

TEACHING

Teaching at Wayne State University

Undergraduate Students

Instructor. Department of Biological Sciences – BIO 3990: Undergraduate course primarily for biology majors who wish to continue in a field beyond that covered in regular courses under the direction of Biological Sciences faculty.

Instructor and Advisor. Department of Physiology – PSL 5010: Undergraduate course involving student participation in laboratory research in the physiological sciences under the supervision of a departmental faculty advisor.
This course involves an introduction to experimental protocol and current related scientific literature.

Advisor. Department of Biological Sciences – BIO 6990: Undergraduate course for honors students involving student participation in laboratory research in the physiological sciences under the supervision of a departmental faculty advisor.

Graduate Students

Instructor. Interdisciplinary Biomedical Sciences – IBS 7060: Biomedical Endocrine and Reproductive Systems Development.
This course is for graduate students within the Ph.D. Program in Anatomy and Cell Biology of which has the aim of providing a broad based knowledge of the important areas of biomedical research.

Instructor. Department of Physiology with Concentration in the Reproductive Sciences Program (PhD) – RPS 7350: Biomolecular Techniques: From Genes to Protein

Instructor. Department of Physiology with Concentration in the Reproductive Sciences Program (PhD), Principles of Reproductive Biology – PSL 7690: Cancers in Reproductive Organs/ Journal Club.
This lecture explains the impact of cancer in women; to discuss the epidemiology, risk factors, screening modalities and preventative strategies of gynecologic cancers and the role of stem cells.

Instructor. Current Research Topics in the Reproductive Sciences – PSL 7775: Molecular Mechanisms of Postoperative Adhesions.
This course is for graduate students within the Ph.D. Program in Physiology with Concentration in the Reproductive Sciences of which covers current research topics in reproductive sciences. The Program itself incorporates the teaching, research and physical resources of both the Physiology and the Obstetrics and Gynecology Departments, offering interdisciplinary doctoral training in a clinical environment in the reproductive sciences. The primary academic focus engages teaching and research training in reproduction and development, with an emphasis on the following: developmental biology, perinatal biology, reproductive endocrinology, reproductive genetics, toxicology/teratology and molecular biology including genomics, proteomics, and bioinformatics. Dissertation research is under the mentorship of Obstetrics and Gynecology basic science graduate faculty.

Advisor and Mentor. Current Research Topics in the Reproductive Sciences – PSL 7996: Arranged Research.
This course is for the graduate students within the "Ph.D. Program in Physiology with Concentration in the Reproductive Sciences" (as described in PSL 7775) which covers graduate level experiences in research techniques. It is required that special research topics, within specified areas, be agreed upon between individual faculty members and students.

Advisor and Mentor. Doctoral Candidate Status I-IV – PSL 9991, 9992, 9993, 9994: Thesis/Dissertation Research and Design.
This course is for the graduate students within the "Ph.D. Program in Physiology with Concentration in the Reproductive Sciences" (as described in PSL 7775). Required in consecutive academic-year semesters following advancement to Ph.D. candidacy status I through IV.

Advisor and Mentor. Doctoral Candidate Dissertation Research and Direction – PSL 9995: Candidate Maintenance Status.
This course is for the graduate students within the "Ph.D. Program in Physiology with Concentration in the Reproductive Sciences" as described above in PSL 7775. Required after completion of 30 credits in PSL 9991-9994.

Director. Summer Reproductive Technology Course. The CS Mott Center for Human Growth and Development, Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, 2014-2015.
The course design is to allow for Reproductive Endocrinology and Infertility/Medical Genetics fellows, as well as graduate students to become familiar with laboratory techniques in the reproductive sciences. The graduate students will acquire a thorough understanding of the

theory and special methodology utilized to perform techniques indicative of reproductive endocrinology and infertility.

Lecturer. Laboratory Techniques. Summer Reproductive Technology Course. The CS Mott Center for Human Growth and Development, Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, 2014.
This lecture explains the various laboratory techniques, and their limitations, as applied to the reproductive sciences.

Lecturer. Molecular Biological Procedures. Summer Reproductive Technology Course. The CS Mott Center for Human Growth and Development, Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, 2015.
This lecture explains the various laboratory techniques, and their limitations, as applied to the reproductive sciences.

Residents and Fellows

Director. Summer Reproductive Technology Course. The CS Mott Center for Human Growth and Development, Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, 2014-2015.
The course design is to allow for Reproductive Endocrinology and Infertility/Medical Genetics fellows, as well as graduate students to become familiar with laboratory techniques in the reproductive sciences. The fellows will acquire a thorough understanding of the theory and special methodology utilized to perform techniques indicative of reproductive endocrinology and infertility.

Instructor. PCR Technique: Concept and Clinical Application Course. The CS Mott Center for Human Growth and Development, Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, 2012-Present.
This course is designed to allow departmental residents, fellows, Reproductive Endocrinology and Infertility/Medical Genetics fellows, and interested graduate students (within the C.S. Mott Center) to become familiar with the PCR technique and how to use it effectively within the laboratory.

Teaching at Other Institutions

Undergraduate Students

Adjunct Associate Professor. Taught two undergraduate courses, CHM104 “Introduction to Chemical Principles” and CHM201 “Introduction to Organic and Biological Chemistry” for nursing and health sciences students at the Department of Chemistry, Oakland University, Rochester, MI, 1991-2004.

Graduate Students

Instructor. Four-day workshop: PCR Techniques, Concepts and Applications. Howard Hughes Research Program, Oakland University, Rochester, MI, May 19-22, 1998.
This workshop was for graduate, postdoctoral, laboratory research personnel, and faculty within the field of science and research.

Instructor. Taught a graduate course CHM554 “Molecular Biology and Biotechnology” at the Department of Chemistry, Oakland University, Rochester, MI, 1995-1998.

Instructor. Biotechnology: From Genes to Proteins. Department of Dermatology, Oakland University, Rochester, MI, 1993-1998.
This course was part of the Research Training in Biotechnology Program postgraduate curriculum for residents and fellows to utilize state-of-the-art molecular technology techniques to answer questions related to molecular pathogenesis of skin diseases such as skin cancer, fibrosis and wound healing.

Teaching Assistant. Introduction to Chemical Principals. Department of Chemistry, University of Essex, Colchester, England, United Kingdom, 1987-1988.

Residents and Fellows

Instructor and Laboratory Advisor. Biotechnology Research Training. Department of Dermatology, Oakland University, Rochester, MI, 1993-1998.
This program trained dermatology residents to utilize state-of-the-art molecular technology techniques to answer questions related to molecular pathogenesis of skin diseases such as skin cancer, fibrosis and wound healing.

Mentorship

Mentor on research projects related to endometriosis, postoperative adhesions, and ovarian cancer to the Department of Obstetrics and Gynecology past and present undergraduate and graduate students, residents, clinical and postgraduate fellows, scholars, faculty, and research technicians, assistants and associates.

Undergraduate Students:

Yousif Abbiss; Newaj Abdullah; Dana Abufarha, Shadi Abuolba Ahmad [awarded the 2007 Wayne State University School of Medicine Undergraduate Research Scholarship Award]; Ali Alarab; Radi Al-Dasouqi; Danna Al-Hadidi; Jeremy Berman; Chelsea Fortin; Ellory Greenberg; Waseem Imann; Shucni Jain; Marisa Karcz; Hadil Katato; Reem Khazaal; Yanamandra Krishnakant;, Wasfeh Musheinish; Bailey Neubauer; Osama Nusrat; Tessy Oommen; Norman Orabi; Alex Papadellis; Sonica Rehan; James Waleke [WSU School of Medicine 2004 graduate]; Rani Yaldo, Yousif Younan; Nabaa Zalzala; and Xuping (Sherry) Zhu.

Graduate:

Osama Nusrat, MD (Master/past): Nusrat O, Belotte J, Fletcher NM, Memaj I, Saed MG, Diamond MP, **Saed GM**. The role of angiogenesis in the persistence of chemoresistance in epithelial ovarian cancer. Reproductive Sciences 23(11):1484-1492, 2016. PMID: 27122375

Batoul Abdullah, PhD: Abdallah BY, Horne SD, Stevens JB, Liu G, Ying AY, Vanderhyden B, Krawetz SK, Gorelick R, Heng HH (2013). Single cell heterogeneity: Why unstable genomes are incompatible with average profiles. Cell Cycle 12:3640-3649, 2013. PMID: 24091732 PMCID: PMC3903715

Jimmy Belotte, MD, PhD: Belotte J, Fletcher NM, Saed MG, Abusamaan MS, Dyson G, Diamond MP, **Saed GM**. A single nucleotide polymorphism in catalase is strongly associated

with ovarian cancer survival. PLoS One 10(8):e0135739, 2015. eCollection 2015. PMID: 26301412 PMCID: PMC4547699

Nicole Fletcher-King, PhD: Fletcher NM, Belotte J, Saed MG, Memaj I, Diamond MP, Morris RT, **Saed GM**. Specific point mutations in key redox enzymes are associated with chemoresistance in epithelial ovarian cancer. Free Radical Biology and Medicine 102:122-132, 2017. PMID: 27890641

Jennell White, PhD: White JC, Jiang ZL, Diamond MP, **Saed GM**. Macrophages induce the adhesion phenotype in normal peritoneal fibroblasts. Fertility and Sterility 96(3):758-763.e3, 2011. Epub July 27, 2011. PMID: 21794857

Residents

Drs. (MD) Zeynep Alpay, Dana Ambler, Tarek Dbouk, Eslam Elhammady, and Valerie Shavell.

Clinical and Postgraduate Fellows:

Drs. (MD) Mazen Abdallah, Awoniyi Awonuga [faculty], Jashoma Banerjee, Alan Bolnick, Jay Bolnick, Subodhsingh Chauhan, Laura Detti, Michael Freeman, April Gago, Roohi Jeelani, Sana Khan, Mohamed Mitwally, Valerie Shavell, Mili Thakur, Rahi Victory, and Terri Woodard; and Christopher Bryant, MD, Associate Professor, Division of Gynecologic Oncology (past faculty).

Of note, the aforementioned have participated in premier annual scientific meetings of the American Society for Reproductive Medicine, Society for Free Radical Biology and Medicine, Society for Reproductive Investigation, and American College of Obstetrics and Gynecology, just to name a few, as well as publishing their many scientific achievements (articles and abstracts) in preeminent peer-reviewed journals (see Publications section).
Acknowledgement: Michael Freeman, MD [past fellow], was awarded a $20,000 research grant from the American Gynecologic and Obstetrical Society (AGOS) during his fellowship [1999-2002]. Alan Bolnick, MD and Sana Khan, MD [past fellows, 2013-2016] were each awarded from the Pacific Coast Reproductive Society, the 2015 Travel Award, as well as Roohi Jeelani, MD and Mili Thakur, MD [past fellows, 2015-2017 and 2014-2017, respectively] who were each awarded the 2016 Travel Award. These AGOS travel awards paid for registration to the annual meeting, course fees, and all travel expenses incurred.

Lastly, Mili Thakur, MD [past fellow, 2014-2017] of the combined Reproductive Endocrinology and Infertility and Medical Genetics Fellowship program (the only one of its kind in the country), was the recipient of the 2016 Pfizer-SRI (Society for Reproductive Investigation), President's Presenter's Award. This award for given to Mili for her abstract entitled, "*Galactose and Its Metabolites Deteriorate Metaphase II Mouse Oocyte Quality through a Mechanism that Involves the Generation of Reactive Oxidative Species, Mitochondrial Dysfunction and Apoptosis*." The President's Presenter's Award is given in recognition of the 25 most meritorious abstracts (either poster or oral presentation) submitted by individuals still in training. Dr. Thakur received this prestigious award at the 63rd Annual Meeting of the Society for Reproductive Investigation, Montreal, Quebec, Canada, in March of 2016.

Scholars

Iyad Ali, PhD: Assistant Professor of Biochemistry, Faculty of Medicine and Health Sciences, An-Najah National University, Nablus, Palestine; visiting Fulbright Arab Fund Fellowship Scholar in the laboratories of Drs. Husam Abu-Soud and Ghassan Saed, Division of Reproductive

Endocrinology and Infertility, Department of Obstetrics and Gynecology, Wayne State University School of Medicine.

Awoniyi Awonuga, MD: Associate Professor, Women's Reproductive Health Research (WRHR) Scholar, Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, Wayne State University School of Medicine. Citation: Awonuga AO, Belotte J, Abuanzeh S, Fletcher NM, Diamond MP, **Saed GM**. Advances in the pathogenesis of adhesion development: the role of oxidative stress. Reproductive Sciences 21(7):823-836, 2014. Epub February 11, 2014. Review. PMID: 24520085 PMCID: PMC4107571

Jimmy Belotte, MD, PhD: Assistant Professor, Women's Reproductive Health Research (WRHR) Scholar, Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, Wayne State University School of Medicine. Citation: *Belotte J, *Fletcher NM, *Alexis M, Morris RT, Munkarah AR, Diamond MP, **Saed GM**. Sox2 gene amplification significantly influences overall survival in serous epithelial ovarian cancer. Reproductive Sciences 22(1):38-46, 2015. Epub July 18, 2014. PMID: 25038052 PMCID: PMC4275450

Lylia Fahmy, MD: Clinical Instructor, Women's Reproductive Health Research (WRHR) Scholar, Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, Wayne State University School of Medicine. Thesis: Effect of Ovarian Hormones on Adhesion Development. 2005.

Faculty

Mentor of current and past Obstetrics and Gynecology clinical faculty through collaborations on research projects and grant submissions. Faculty members are as follows: Awoniyi Awonuga, MD, Professor, Division of Reproductive Endocrinology and Infertility and Women's Reproductive Health Research (WRHR) Scholar (training completed December 2015); Jimmy Belotte, MD, Associate Professor, Division of Gynecology, Women's Reproductive Health Research (WRHR) Scholar, (training completed September 2016 with PhD); Lylia Fahmy, MD, past Clinical Instructor, Division of Reproductive Endocrinology and Infertility, Women's Reproductive Health Research (WRHR) Scholar, (training completed 2005); and Peter Baumann, MD, Associate Professor, Division of Gynecology (retired).

I have also been instrumental to key professional presentations at local, national, and international conferences by our past and present senior faculty members of the Obstetrics and Gynecology Department. They are as follows: Adnan Munkarah, MD, Professor and Director, Division of Gynecologic Oncology; Bernard Gonik, MD, Professor, Division of Maternal and Fetal Medicine; Jay Berman, MD, Associate Professor and Associate Chair, Department of Obstetrics and Gynecology and Director, Division of Gynecology; John Malone, Jr, MD, Professor and past Chair, Department of Obstetrics and Gynecology (deceased); Kamran Moghissi, MD, Professor Emeritus, past Chair Emeritus, Department of Obstetrics and Gynecology, past Director, Division of Reproductive Endocrinology and Infertility, and past Director, CS Mott Center for Human Growth and Development (retired); and Michael Diamond, MD, Professor, past Associate Chair, Department of Obstetrics and Gynecology, past Director, Division of Reproductive Endocrinology and Infertility, and past Assistant Dean of Clinical and Translational Research, Wayne State University School of Medicine (now at Georgia Regents University, Augusta, GA).

Research Associates/Assistants/Technicians

In the laboratory of Dr. Ghassan Saed: Drs. (PhD) Boytcho Boytchev, Semira Galijasevic, Zhongliang (John) Jiang, MD, Hong Lu, Qui Lu, Gheorghe Proteasa, Natalie Rizk, Rona Wang, MD, and Ming Zhao, MD; Danielle Hall, BS, Nicole Fletcher-King, BS, MS, and Manal Omar, BS.

Essays/Theses/Dissertations Directed

Name: Osama Nusrat, MD (Master Degree/past), Department of Physiology and Reproductive Sciences (2015-2017), Wayne State University School of Medicine, Detroit, MI.

Dissertation Title: The Role of Angiogenesis in the Persistence of Chemoresistance in Epithelial Ovarian Cancer

Date Awarded: September 2017

Current Status: Resident, Department of Internal Medicine, University of Arizona College of Medicine, Tucson, AZ

Name: Jimmy Belotte, MD, PhD, Department of Physiology in the Reproductive Sciences Concentration (2012-2016); and Women's Reproductive Health Research (WRHR) Scholar, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI

Dissertation Title: The Role of Oxidative Stress in the Establishment of Resistance to Cisplatin in Epithelial Ovarian Cancer Cells

Date Awarded: September 14, 2016 and WRHR training completed September 14, 2016

Current Status: Associate Professor, Division of Gynecology, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI

Name: Batoul Abdullah, PhD, Department of Physiology in the Center for Molecular Medicine and Genetics Concentration (2012-2016), Wayne State University School of Medicine, Detroit, MI

Dissertation Title: Fuzzy Inheritance: A Novel Form of Somatic Cell Inheritance that Regulates Cell Population Heterogeneity

Date Awarded: 2016

Current Status: Postdoctoral Fellow in the laboratory of Henry (Hong-Qiang) Heng, PhD, Center for Molecular Medicine & Genetics and Pathology, Wayne State University School of Medicine, Detroit, MI

Name: Awoniyi Awonuga, MD, Women's Reproductive Health Research (WRHR) Scholar, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI

Thesis Title: Oxidative Stress in the Pathogenesis of Post-Operative Adhesions

Training Completed: December 2015

Current Status:	Professor and Interim Director, Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI
Name:	Nicole Fletcher-King, PhD, Department of Physiology in the Reproductive Sciences Concentration Program (2008-2013), Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI
Dissertation Title:	The Role of Oxidative Stress in the Pathogenesis of Epithelial Ovarian Cancer
Date Awarded:	September 2013
Current Status:	Postdoctoral Fellow in the laboratory of Ghassan M Saed, PhD, Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, CS Mott Center for Human Growth and Development, Wayne State University School of Medicine, Detroit, MI
Name:	Jennell White, PhD, Department of Physiology in the Reproductive Sciences Concentration Program (2000-2011), Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI
Dissertation Title:	The Potential Role of Innate Immunity in the Pathogenesis of Postoperative Adhesions
Date Awarded:	September 2011
Current Status:	Postdoctoral Fellow, Department of Pediatrics, Wayne State University School of Medicine, Detroit, MI
Name:	Lylia Fahmy, MD, Women's Reproductive Health Research (WRHR) Scholar, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI
Thesis Title:	Effect of Ovarian Hormones on Adhesion Development
Date Completed:	September 2005
Current Status:	Associate Professor, Department of Obstetrics and Gynecology, University of Nebraska Medical Center, Omaha, NB

Course or Curriculum Development

Originator and Director. Summer Reproductive Technology Course. 2014
This course design is to allow for Reproductive Endocrinology and Infertility/Medical Genetics fellows, as well as graduate students, to become

familiar with all aspects of laboratory techniques within the field of reproductive sciences. Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, The C.S. Mott Center for Human Growth and Development, Wayne State University School of Medicine, Detroit, MI.

Course Director. Reproductive Sciences Concentration – RPS 7350: Biomolecular Techniques: From Genes to Protein. 2006
This course design is specifically for graduate students enrolled in the PhD Program in Physiology with Concentration in the Reproductive Sciences, as part of their curriculum. This is an integrated PhD program incorporating the teaching, research, and physical resources of two departments -- Physiology and Obstetrics & Gynecology at Wayne State University School of Medicine, Detroit, MI.

Organizer. Four-day workshop (May 19-22): PCR Techniques, Concepts, and Applications. 1998
Workshop developed for undergraduates, graduates, postdoctoral, laboratory personnel, and faculty studying and/or working within the field of science and research. Sponsored by the Howard Hughes Research Program of Oakland University, Rochester, MI.

Designer. Introduction to Molecular Cloning. 1996
Course designed to teach techniques for characterization and manipulation of DNA and RNA from the basis of modern biomedical research. Coursework pertinent towards medical residents and fellows at the Henry Ford Hospital, Detroit, MI, and graduate students at Oakland University, Rochester, MI.

Designer. Research Training in Biotechnology. 1993
This program trained Department of Dermatology residents and fellows to utilize state-of-the-art molecular technology techniques to answer questions related to molecular pathogenesis of skin diseases such as skin cancer, fibrosis and wound healing at Henry Ford Hospital, Detroit. MI. This training ended in 1998.

Course Director. I have participated in developing the course, Introduction to Chemical Principles (CHM 104) to meet general education requirements. CHM 104 satisfies the university general education requirement in natural science and technology (NST). The learning outcomes for NST courses state that the student will demonstrate knowledge of major concepts from natural science or technology, including developing and testing of hypotheses, drawing conclusions, and reporting of findings through some laboratory experience or an effective substitute. This course taught at Oakland University, Rochester, MI. 1991–2004

Designer. Laboratory course. I was actively involved in developing and instructing two laboratory sections for CHM 104. Students learned how to evaluate sources of information in science or technology. Developed at Oakland University, Rochester, MI 1991–2004

Designer. I developed and taught CHM 104 and CHM 201 to nursing students 2005–2010

on-line (a web-based instruction). I designed courses to satisfy the university general education requirement in natural science and technology (NST). For this, I utilized and implemented the virtual chemistry laboratory experience to be an integral part of this course. Developed at Oakland University, Rochester, MI,

GRANTS, CONTRACTS, AND OTHER FUNDING:

Active National/International Grants and Contracts

Role: Mentor, Percent Effort: 0%; Principal Investigator: NM King, PhD
Title: "Novel Biomarkers for Early Detection of Ovarian Cancer." The project's design is to identify key markers of oxidative stress that have the potential to serve as screening tools for ovarian cancer and may play a role in the acquisition of chemoresistance.
Source: Prevent Cancer Foundation, Postdoctoral Fellowship Grant
Date: 01/01/16 – 12/31/18
Total Direct Costs: $80,000

Role: Principal Investigator, Percent Effort: 5%
Title: "Elucidation of Cellular Mechanisms of Evitar of Post-Operative Fibrosis."
Source: Temple Therapeutics, 25S8P1
Date: 04/01/17 – 05/31/18
Total Direct Costs: $100,000

Pending National/International Grants and Contracts

Role: Mentor, Percent Effort: 0%; Principal Investigator: NM King, PhD
Title: "Novel Mechanism of Apoptosis in Chemoresistant Ovarian Cancer Cells." To determine whether chenoresistance in ovarian cancer manifests decreased apoptosis through enhanced s-nitrosylation of caspase-3 mechanism which can, thereby, be reversed by DCA.
Source: American Association for Cancer Research (AACR)
Date: 07/01/17 – 06/30/19
Total Direct Costs: $100,000

Role: Principal Investigator, Percent Effort: 30%
Title: "Identification of a Novel Target with Intriguing Anti-Tumorigenic Effects in Ovarian Cancer." To identify and test a target that cross-reacts with the CD11b antibody and determines its efficacy in killing both sensitive and chemoresistant ovarian cancer cells.
Source: NIH/NICHD R01, Proposal #17-0220
Date: 09/01/17 – 08/31/22
Total Direct Costs: $1,919,600

Role: Mentor, Percent Effort: 0%; Principal Investigator: NM King, PhD
Title: "Novel Marker of Survival in Ovarian Cancer Cells." To test the anti-tumorigenic potential of integrin αV/β1 antibodies in sensitive and chemoresistant ovarian cancer.
Source: U.S. Department of Defense (DOD)
Date: 01/01/18 – 12/31/19
Total Direct Costs: $385,000

Role: Principal Investigator, Percent Effort: 25%
Title: "Cross-Talk Between MPO and iNOS Regulates Apoptosis in Chemoresistant Ovarian Cancer." To determine whether chemoresistance in ovarian cancer manifests decreased apoptosis through enhanced s-nitrosylation of caspase-3 mechanism, which can be reversed by DCA.
Source: NIH/NICHD R21
Date: 09/01/17 – 08/31/19
Total Direct Costs: $423,500

Role: Principal Investigator, Percent Effort: 10%
Title: "A Novel Target with Intriguing Anti-Tumorigenic Effects in Cancer." To identify and test a target that cross-reacts with the CD11b antibody and determines its efficacy in killing both sensitive and chemoresistant ovarian cancer cells.
Source: NIH/DHHS Small Business Technology Transfer Grant (STTR), R41
Date: 07/01/17 – 6/30/18
Total Direct Costs: $299,999

Role: Principal Investigator, Percent Effort: NA
Title: "A Novel Target with Intriguing Anti-Tumorigenic Effects in Cancer." To identify and test a target that cross-reacts with the CD11b antibody and determines its efficacy in killing both sensitive and chemoresistant ovarian cancer cells.
Source: The Honorable Tina Brozman Foundation, Inc. for Ovarian Cancer Research – Letter of Intent
Date: 2017
Total Direct Costs: $100,000

Role: Principal Investigator, Percent Effort: 5%; Co-Principal Investigator: NM King, PhD
Title: "Potential Anti-Tumorigenic Antigen for Cancer Therapy." To identify and test a target that cross-reacts with the CD11b antibody and determines its efficacy in killing both sensitive and chemoresistant ovarian cancer cells.
Source: Elsa U. Pardee Foundation Grant Program, Proposal #17-0715
Date: 01/01/18 – 12/31/18
Total Direct Costs: $187,958

Role: Principal Investigator, Percent Effort: NA
Title: "A Novel Target with Intriguing Anti-Tumorigenic Effects in Cancer." To identify and test a target that cross-reacts with the CD11b antibody and determines it efficacy in killing both sensitive and chemoresistant ovarian cancer cells.
Source: Ovarian Cancer Research Fund Alliance, Inc. (OCRFA)
Date: 01/01/18 – 12/31/20
Total Direct Costs: $300,000

Role: Mentor, Percent Effort: 0%; Principal Investigator: NM King, PhD
Title: "Antitumor Effects of Targeting Integrin αV/β1 in Ovarian Cancer Cells." To test the anti-tumorigenic potential of integrin αV/β1 antibodies in ovarian cancer patient samples.
Source: Ovarian Cancer Research Fund Alliance, Inc., Ann Schreiber Mentored Investigator Award
Date: 01/01/18 – 12/31/18

Total Direct Costs: $75,000

Pending Other Grants and Contracts

Role: Principal Investigator
Title: "Repurposing ABCIXIMAB, A Clinically Approved Anticoagulant for the Treatment of Ovarian Cancer." To determine whether abciximab is an effective therapy against sensitive and resistant ovarian cancer.
Source: Michigan Ovarian Cancer Alliance (MIOCA)
Date: 04/01/17 – 03/31/18
Total Direct Costs: $50,000

Role: Principal Investigator
Title: "ReoPro and Ovarian Cancer."
Source: Michigan Ovarian Cancer Alliance (MIOCA)
Date: 04/01/17 – 03/31/18
Total Direct Costs: $50,000

Role: Principal Investigator
Title: "A Novel Target with Intriguing Anti-Tumorigenic Effects in Cancer."
Source: DS Biotech, LLC, Proposal #17-0289
Date: 07/01/17– 06/30/18
Total Direct Costs: $100,000

Submitted National/International Grants and Contracts

Role: Principal Investigator
Title: "A Novel Target with Intriguing Anti-Tumorigenic Effects in Ovarian Cancer."
Source: Rivkin Center for Ovarian Cancer, Pilot Study Awards, 573569

Previously Funded Grants and Contracts

Role: Co-Principal Investigator; Principal Investigators: MP Diamond, MD, EN Kraiselburd, PhD
Title: "WSU-UPR Research Partnership to Promote Diversity in the Reproductive Sciences"
Source: NIH/NICHD, HD-09-008
Date: 08/2010 – 07/2015
Total Direct Costs: $3,020,000

Role: Co-Principal Investigator, Principal Investigator: MP Diamond, MD
Title: "WSU Clinical and Translational Science Award Planning Grant"
Source: NIH/NICHD, 1P20 RR 023578
Date: 09/2006 – 09/2012
Total Direct Costs: $2,225,750

Role: Consultant; Principal Investigator: MP Diamond, MD
Title: "WSU Cooperative Reproductive Medicine Network Center"
Source: NIH/NICHD, U10 HD-39005
Date: 08/2007 – 07/2012
Total Direct Costs: $1,510,000
Role: Principal Investigator, Percent Effort: 3.60%

Title: "Postoperative Adhesion: Roles of Hypoxia and Nitric Oxide"
Source: NIH/NICHD, Division of Pharmacology, Physiology, and Biological Chemistry, 1R01 GM069941-01A3
Date: 10/01/06 – 09/30/12
Total Direct Costs: $1,312,500

Role: Mentor; Principal Investigator: J White, MS, PhD Candidate (WSU)
Title: "Post-Operative Adhesions: Roles of Hypoxia in Nitric Oxide"
Source: NIH/NICHD, Minority Research Supplemental Award, 3R01GM069941-02S1
Date: 01/01/08 – 08/31/10
Total Direct Costs: $151,441

Role: *Principal Investigator
Title: "*CUAAH Subcontract – Specialty Laboratory Core"
Date: 06/01/08 – 05/31/10
Total Direct Costs: $403,840

Principal Investigator: JM Flack, MD
Title: "Center for Urban African American Health (CUAAH)"
Source: NIH/NIEHS
Date: 06/01/07 – 05/31/10
Total Direct Costs for Center: $9,487,709

Role: Principal Investigator
Title: "Angiogenesis of Ovarian Cancer"
Source: Frank Iacobell Endowed Chair, Department of Obstetrics and Gynecology, Wayne State University School of Medicine
Date: 01/01/08 – 12/31/09
Total Direct Costs: $41,500

Role: Co-Principal Investigator; Principal Investigator: R Kannan, PhD
Title: "Wayne State University, Department of Engineering – Subcontract"
Source: President's Research Award, Technology and Transfer Office
Date: 01/01/08 – 12/31/09
Total Direct Costs: $15,000

Role: Consultant; Principal Investigator: MP Diamond, MD U10 HD-39005
Title: "WSU Cooperative Reproductive Medicine Network Center"
Source: NIH/NICHD
Date: 04/01/00 – 03/31/07
Total Direct Costs: $1,349,994

Role: Principal Investigator; Co-Principal Investigator: MP Diamond, MD
Title: "Testing of Perfluorodecalin for Adhesion Prevention"
Source: Novel Pharma, Inc.
Date: 11/01/01 – 06/30/02
Total Direct Costs: $32,000

Role: Principal Investigator; Co-Principal Investigator: MP Diamond, MD
Title: "Effect of Tissel on Human Peritoneal Fibroblasts"
Source: Baxter Research Grant
Date: 09/30/01 – 12/31/02
Total Direct Costs: $98,000

Role: Co-Principal Investigator; Principal Investigator: MP Diamond, MD
Title: "Why Does Endometriosis Cause Adhesions?"
Source: Endometriosis Association
Date: 01/01/01 – 12/31/01
Total Direct Costs: $38,000

Role: Co-Principal Investigator; Principal Investigator: MP Diamond, MD
Title: "Effect of Tissel on Human Mesothelial Cell Culture"
Source: Baxter Research Grant
Date: 01/01/01 – 08/31/01
Total Direct Costs: $60,000

Role: Principal Investigator
Title: "The Effects of Hypoxia on the Levels of Peritoneal ECM Proteins"
Source: Wayne State University Department of Obstetrics and Gynecology, Interdepartmental Research Grant
Date: 03/01/98 – 12/31/00
Total Direct Costs: $19,000

Role: Principal Investigator
Title: "The Role of p53 in the Pathogenesis of Keloids"
Source: Henry Ford Hospital Small Project Award
Date: 01/01/98 – 12/31/98
Total Direct Costs: $20,000

Role: Principal Investigator
Title: "Patterns of Cytokine Expression in Cutaneous T-Cell Lymphoma"
Source: Henry Ford Hospital Small Project Award
Date: 01/01/93 – 12/31/94
Total Direct Costs: $20,000

Previously Submitted, Not Funded Grants and Contracts

Role: Principal Investigator, Percent Effort: 20%
Title: "Novel Mechanisms of Apoptosis in Chemoresistant Ovarian Cancer Cells." To determine whether chenoresistance in ovarian cancer manifests decreased apoptosis through enchanged s-nitrosylation of caspase-3 mechanism, which can be reversed by DCA.

Source: NIH/NICHD, R21
Date: 04/01/17 – 03/31/19
Total Direct Costs: $423,500

Role: Principal Investigator
Title: "Novel Mechanisms of Apoptosis in Chemoresistant Ovarian Cancer Cells." To determine whether chenoresistance in ovarian cancer manifests decreased apoptosis through enchanged s-nitrosylation of caspase-3 mechanism, which can be reversed by DCA.
Source: Elsa U. Pardee Foundation Grant Program
Date: 01/01/17 – 12/31/17
Total Direct Costs: $113,966

Role: Mentor, Percent Effort: 0%; Principal Investigator: NM King, PhD
Title: "Novel Mechanisms of Apoptosis in Chemoresistant Ovarian Cancer Cells." The project's design is to determine whether chemoresistance in ovarian cancer manifests decreased apoptosis through enhanced s-nitrosylation of caspase-3 mechanism, which can be reversed by DCA.
Source: NIH/NICHD, R03
Date: 12/01/16 – 11/30/18
Total Direct Costs: $50,000

Role: Principal Investigator
Title: "Innovative New Target for Ovarian Cancer Therapy." The project was designed to identify and test a target that cross-reacts with the CD11b antibody and determines its efficacy in killing both sensitive and chemoresistant ovarian cancer cells.
Source: The Honorable Tina Brozman Foundation, Inc. for Ovarian Cancer Research
Date: 08/01/16 – 07/31/18
Total Direct Costs: $200,000

Role: Principal Investigator
Title: "Redox Enzyme-Mediated Prosurvival of Chemoresistance in Ovarian Cancer." To determine whether development of chenoresistance in ovarian cancer is attributed to enhanced oxidative stress leading to a genotype switch in key oxidant and antioxidant enzymes.
Source: Ovarian Cancer Research Fund Alliance, Inc. (OCRFA)
Date: 2016 – 2019
Total Direct Costs: $900,000

Role: Mentor, Percent Effort: 0%; Principal Investigator: NM King, PhD
Title: "Chemoresistant Ovarian Cancer Cells Manifest Lower Vascular Endothelial Growth Factor and Hypoxia Inducible Factor-1α: A Potential Survival Mechanism." The design of the project was to determine whether VEGF and HIF-1α contribute to the persistence of chemoresistance in ovarian cancer.
Source: Ovarian Cancer Research Fund, Ann Schreiber Mentored Investigator Award
Date: 2016 – 2017
Total Direct Costs: $75,000

Role: Mentor, Percent Effort: 0%; PI: NM King, PhD
Title: "Novel Biomarkers for Early Detection of Ovarian Cancer." The design of the project was to determine whether MPO and free iron could be utilized as biomarkers for the early detection of ovarian cancer.
Source: NIH/NICHD, R03 – Resubmission of scored proposal

Date: 12/01/15–11/30/17
Total Direct Costs: $153,583

Role: Principal Investigator, Percent Effort: 30%
Title: "Redox Enzyme-Mediated Prosurvival of Chemoresistance in Ovarian Cancers." The design of the project was to determine whether development of chemoresistance in ovarian cancer is attributed to enhanced oxidative stress leading to a genotype switch in key oxidant and antioxidant enzymes.
Source: NIH/NICHD, R01
Date: 12/01/15 – 11/30/20
Total Direct Costs: $2,494,526

Role: Mentor, Percent Effort: 0%; PI: NM King, PhD
Title: "Novel Biomarkers for Early Detection of Ovarian Cancer." The design of the project was to determine whether MPO and free iron could be utilized as biomarkers for the early detection of ovarian cancer.
Source: NIH/NICHD, R03
Date: 11/01/14 – 10/31/16
Total Direct Costs: $152,000

Role: Principal Investigator, Percent Effort: 30%
Title: "Chemoresistance Induces a Genotype Switch in Redox Enzymes in Ovarian Cancer." The design of the project was to determine whether development of chemoresistance in ovarian cancer is attributed to enhanced oxidative stress leading to a genotype switch in key oxidant and antioxidant enzymes.
Source: NIH/NICHD, R01
Date: 04/ 01/15 – 03/31/20
Total Direct Costs: $3,124,495

Role: Mentor, Percent Effort: 0%; Principal Investigator: NM King, PhD
Title: "Biomarkers for Early Detection of Ovarian Cancer." The design of the project was to determine whether MPO and free iron could be utilized as biomarkers for the early detection of ovarian cancer.
Source: Sandy Rollman Ovarian Cancer Foundation (SROCF) Fellowship
Date: 06/01/14 – 05/31/15
Total Direct Costs: $50,000

Role: Mentor, Percent Effort: 0%; Principal Investigator: NM King, PhD
Title: "Novel Biomarkers for Early Detection of Ovarian Cancer." The design of the project was to determine whether MPO and free iron could be utilized as biomarkers for the early detection of ovarian cancer.
Source: Ladies Auxiliary to the Veterans of Foreign Wars, Postdoctoral Cancer Research Fellowship
Date: 06/01/14 – 05/31/16
Total Direct Costs: $50,000

Role: Mentor, Percent Effort: 0%; PI: NM King, PhD
Title: "Novel Biomarkers for Early Detection of Ovarian Cancer." The design of the project was to determine whether MPO and free iron could be utilized as biomarkers for the early detection of ovarian cancer.
Source: Kaleidoscope of Hope Foundation, Young Investigator Award

Date: 04/01/14 – 03/31/15
Total Direct Costs: $50,000

Role: Mentor, Percent Effort: 0%; Principal Investigator: NM King, PhD
Title: "Novel Biomarkers for Early Detection of Ovarian Cancer." The design of the project was to determine whether MPO and free iron could be utilized as biomarkers for the early detection of ovarian cancer.
Source: Damon Runyon Cancer Research Foundation
Date: 07/01/14 – 06/30/17
Total Direct Costs: $158,000

Role: Mentor, Percent Effort: 0%; Principal Investigator: NM King, PhD
Title: "Chemoresistance Induces a Genotype Switch in Epithelial Ovarian Cancer Cells." The project was designed to determine whether development of chemoresistance in ovarian is attributed to enhanced oxidative stress leading to a genotype switch in key oxidant and antioxidant enzymes.
Source: American Cancer Society Postdoctoral Fellowship
Date: 01/01/15 – 12/31/18
Total Direct Costs: $163,500

Role: Mentor, Percent Effort: 0%; Principal Investigator: NM King, PhD
Title: "Novel Biomarkers for the Early Detection of Ovarian Cancer." The design of the project was to determine whether MPO and free iron can be utilized as biomarkers for the early detection of ovarian cancer.
Source: American Association for Cancer Research
Date: 2015 – 2016
Total Direct Costs: $50,000

Role: Principal Investigator, Percent Effort: 30%
Title: "Postoperative Adhesion Development is Controlled by Mechanisms that Emanate from a Hypoxia-Induced Genotype Switch in Key Enzymes of Oxidative Stress." Identification of markers that are strongly associated with adhesions and in patients will contribute to both the delineation of mechanisms of adhesion development and serve as potential targets for therapy and intervention.
Source: NIH/NICHD, R01
Date: 07/01/15 – 06/30/20
Total Direct Costs: $1,921,633

Role: Principal Investigator, Percent Effort: 25%
Title: "Combination of Antioxidants Effectively Reduces Adhesion Development." The design of the project was to determine the effects of antioxidants on the prevention of postoperative adhesion development.
Source: NIH/NICHD, R03
Date: 07/01/15 – 06/30/17
Total Direct Costs: $153,314

Role: Mentor, Percent Effort: 0%; Principal Investigator: NM King, PhD
Title: "New Insights into the Pathogenesis of Ovarian Cancer." To identify keymarkers of oxidative stress that have the potential to serve as screening tools for ovarian cancer and may play a role in the acquisition of chemoresistance.
Source: Prevent Cancer Foundation

Date: 04/01/14 – 01/31/16
Total Direct Costs: $80,000

Role: Mentor, Percent Effort: 0%; Principal Investigator: AO Awonuga, MD
Title: "Effects of Dietary Lycopene on Incidence and Severity of Postoperative Adhesions." The design of the project was to determine the effects of antioxidants on the prevention of postoperative adhesion development.
Source: NIH/NICHD, R03
Date: 09/01/14 – 08/31/16
Total Direct Costs: $152,000

Role: Mentor, Percent Effort: 0%; Principal Investigator: NM King, PhD
Title: "Novel Biomarkers for Detection of Early Ovarian Cancer." The design of the project was to determine whether MPO and free iron can be utilized as biomarkers for the early detection of ovarian cancer.
Source: Marsha Rivkin Center for Ovarian Cancer Research, Scientific Scholar Award – Postdoctoral Fellowship
Date: 04/01/14 – 03/31/15
Total Direct Costs: $60,000

Role: Mentor; Percent Effort: 0%; Principal Investigator: J Belotte, MD
Title: "Catalase SNP as a Genetic Predictor for Epithelial Ovarian Cancer." The design of the project was to determine whether a SNP in the catalase gene can be utilized as a predictive marker for epithelial ovarian cancer.
Source: Marsha Rivkin Center for Ovarian Cancer Research, Scientific Scholar Award – Postdoctoral Fellowship
Date: 04/01/14 – 03/31/15
Total Direct Costs: $60,000

Role: Mentor, Percent Effort: 0%; Principal Investigator: NM King, PhD
Title: "Novel Biomarkers for the Early Detection of Ovarian Cancer." The design of the project was to determine whether MPO and free iron can be utilized as biomarkers for the early detection of ovarian cancer.
Source: Hope Funds Cancer Research Postdoctoral Fellowship
Date: 2014 – 2016
Total Direct Costs: $100,000

Role: Principal Investigator
Title: "Chemoresistance in Ovarian Cancer Manifests a Genotype Switch in Oxidant Enzymes."
The design of the project was designed to determine whether a genotype switch in key oxidant enzymes is induced in chemotherapy treated ovarian cancer cells and the subsequent effect of the enzymatic activity.
Source: Marsha Rivkin Center for Ovarian Cancer Research; Pilot Study
Date: 04/01/14 – 03/31/15
Total Direct Costs: $75,000

Role: Principal Investigator, Percent Effort: 30%; Co-Investigators: MP Diamond, MD, S Ghamande, PhD
Title: "Chemoresistance Induces a Genotype Switch in Redox Enzymes in Ovarian Cancer."
The design of the project was to determine whether development of chemoresistance in ovarian

cancer were attributed to enhanced oxidative stress leading to a genotype switch in key oxidant and antioxidant enzymes.
Source: NIH/NICHD, R01
Date: 07/01/14 – 06/30/19
Total Direct Costs: $2,932,687

Role: Principal Investigator, Percent Effort: 25%
Title: "Chemoresistance in Ovarian Cancer is Attributed to Enhanced Oxidative Stress." The design of the project was to determine whether development of chemoresistance in ovarian cancer were attributed to enhanced oxidative stress.
Source: NIH/NICHD, R03
Date: 07/01/14 – 06/30/16
Total Direct Costs: $152,000

Role: Principal Investigator, Percent Effort: 25%
Title: "Chemoresistance in Ovarian Cancer Manifests a Genotype Switch in Oxidant Enzymes." The design of the project was to determine whether development of chemoresistance in ovarian cancer were attributed to enhanced oxidative stress leading to a genotype switch in key oxidant and antioxidant enzymes.
Source: NIH/NICHD, R03
Date: 07/01/14 – 06/30/16
Total Direct Costs: $152,000

Role: Mentor, Percent Effort: 0%; Principal Investigator: J Belotte, MD
Title: "Characterization of Epithelial Ovarian Cancer Stem Cells." The design of the project was to determine the role of pluripotency markers in epithelial ovarian cancer and the association with survival.
Source: NIH/NICHD, R03
Date: 09/30/14 – 06/30/16
Total Direct Costs: $152,000

Role: Mentor, Percent Effort: 0%; PI: J Belotte, MD
Title: "Catalase SNP as a Genetic Predictor for Epithelial Ovarian Cancer." The design of the project was to determine whether a SNP in the catalase gene can be utilized as a predictive marker for epithelial ovarian cancer.
Source: NIH/NICHD, R03
Date: 09/30/14 – 08/31/16
Total Direct Costs: $152,000

Role: Principal Investigator, Percent Effort: 20%
Title: "Innovative New Target for Ovarian Cancer Therapy." The project was designed to identify and test a target that cross-reacts with the CD11b antibody and determines its efficacy in killing both sensitive and chemoresistant ovarian cancer cells.
Source: NIH/NICHD, R21
Date: 12/31/16 – 11/30/18
Total Direct Costs: $275,000

Role: Principal Investigator
Title: "Redox Enzyme-Mediated Prosurvival of Chemoresistance in Ovarian Cancer." The design of the project was to determine whether development of chemoresistance in ovarian

cancer were attributed to enhanced oxidative stress leading to a genotype switch in key oxidant and antioxidant enzymes.
Source: Ovarian Cancer Research Fund, Program Project Development Grant
Date: 201 6 – 2019
Total Direct Costs: $900,000

Role: Principal Investigator, Percent Effort: 20%
Title: "Novel Mechanisms of Apoptosis in Chemoresistant Ovarian Cancer Cells." The design of the project was to determine whether chemoresistance in ovarian cancer manifests decreased apoptosis through enhanced s-nitrosylation of caspase-3 mechanism, which can be reversed by DCA.
Source: NIH/NICHD, R21
Date: 12/01/16 – 11/30/18
Total Direct Costs: $275,000

Role: Mentor, Percent Effort 0%; Principal Investigator: NM King, PhD
Title: "Novel Biomarkers for Early Detection of Ovarian Cancer." The design of the project was to determine whether MPO and free iron can be utilized as biomarkers for the early detection of ovarian cancer.
Source: L'Oreal USA for Women in Science Fellowship
Date: 2016 – 2017
Total Direct Costs: $60,000

PATENTS:

Status: Provisional Submission
Date: 2016
Number: WSU
Title: Compositions and Methods Targeting CD11b/CD18, Myeloperoxidase and/or Integrin Alpha and Beta 1 to Treat Solid Tumors
Role: Inventor

Status: Pending
Date: 2015
Number: WSU
Title: Novel Approach to Selectively Kill Cancer Cells
Role: Inventor

Status: Pending
Date: 2008
Number: WSU
Title: Anticancer Vaccine
Role: Inventor

Status: Pending
Date: WSU
Number: WSU 00-492
Title: Prevention of Adhesions
Role: Inventor

Status: Pending
Date: March 18, 2004
Number: WSU
Title: Regulation of Peritoneal Healing and Adhesion Development
Role: Inventor

Status: Pending
Date: June 25, 2002
Number: WSU
Title: Modification of Healing and Adhesion Development
Role: Inventor

PUBLICATIONS

Peer-Reviewed Publications

**Indicates student, trainee, or postdoctoral*

Reports of Original Work

1. **Saed GM**, *Fletcher NM, Diamond MP, Morris RT, Gomez-Lopez N, *Memaj I. Novel expression of CD11b in epithelial ovarian cancer: potential therapeutic target. Gynecologic Oncology 2018 Mar;148(3):567-575. [Epub 2018 Jan 10] PMID: 29329880. *Role: Writer and Mentor*

2. Detti L, *Fletcher NM, **Saed GM**, Peregrin-Alvarez I, Uhlmann RA. Anti-Műllerian Hormone (AMH) may stall ovarian cortex function through modulation of hormone receptors other than the AMH receptor. Reproductive Sciences January 1:19337119117737850, 2017. [Epub ahead of print] PMID: 29141508. *Role: Mentor and collaborator*

3. *Fletcher NM, *Abusamaan MS, *Memaj I, *Saed MG, Al-Hendy A, Diamond MP, **Saed GM**. Oxidative stress: a key regulator of leiomyoma cell survival. Fertility and Sterility 107(6):1387-1394.e1 , 2017. Epub May 5, 2017. PMID: 28483502. *Role: Writer and Mentor*

4. **Saed GM**, Diamond MP, Fletcher NM. Updates of the role of oxidative stress in the pathogenesis of ovarian cancer. Gynecologic Oncology 2017 Jun;145(3):595-602. Epub 2017 Feb 23. Review. PMID:28237618. *Role: Writer and Mentor*

5. *Fletcher NM, *Belotte J, *Saed MG, *Memaj I, Diamond MP, Morris RT, **Saed GM**. Specific point mutations in key redox enzymes are associated with chemoresistance in epithelial ovarian cancer. Free Radical Biology and Medicine 102:122-132, 2017. Epub November 25, 2016. PMID: 27890641. *Role: Mentor and Writer*

6. *Nusrat O, *Belotte J, *Fletcher NM, *Memaj I, *Saed MG, Diamond MP, **Saed GM**. The role of angiogenesis in the persistence of chemoresistance in epithelial ovarian cancer. Reproductive Sciences 23(11):1484-1492, 2016. Epub April 26, 2016. PMID: 27122375 *Role: Mentor and Writer*

7. *Shaeib F, *Khan SN, *Thakur M, Kohan-Ghadr HR, Drewlo S, **Saed GM**, Pennathur S, Abu-Soud HM. The impact of myeloperoxidase and activated macrophages on metaphase II mouse oocyte quality. PLoS One 11(3):e0151160, 2016. eCollection 2016. PMID: 26982351 *Role: Mentor and collaborator*

8. Ahmed RS, Liu G, Renzetti A, Farshi P, Yang H, Soave C, **Saed G**, El-Ghoneimy AA, El-Banna HA, Foldes R, Chan TH, Dou QP. Biological and Mechanistic Characterization of Novel Prodrugs of Green Tea Polyphenol Epigallocatechin Gallate Analogs in Human Leiomyoma Cell Lines. J Cell Biochem. 2016 Oct;117(10):2357-69.doi: 10.1002/jcb.25533. Epub 2016 Mar 28. PMID:26950525. *Role: Collaborator*

9. *Fletcher NM, Awonuga AO, *Abusamaan MS, *Saed MG, Diamond MP, **Saed GM**. Adhesion phenotype manifests an altered metabolic profile favoring glycolysis. Fertility and Sterility 105(6):1628-1637, 2016. Epub February 23, 2016. PMID: 26920255. *Role: Mentor and Writer.*

10. **Saed GM**, *Fletcher NM, Diamond MP. The creation of a model for ex vivo development of postoperative adhesions. Reproductive Sciences 23(5):610-622, 2016. Epub September 25, 2015. PMID: 26408397. *Role: Mentor*.

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Non Peer-Reviewed Publications

Other (On-Line Publications) * Indicates student, trainee, or postdoctoral

1. *Nusrat O, *Belotte J, *Fletcher NM, *Memaj I, *Saed MG, Diamond MP, **Saed GM**. The role of angiogenesis in the persistence of chemoresistance in epithelial ovarian cancer. www.OncToday.com, Beyond the Abstract, June 21, 2016.

2. *Belotte J, *Fletcher NM, *Alexis M, Morris RT, Munkarah AR, Diamond MP, **Saed GM**. Sox2 gene amplification significantly impacts overall survival in serous epithelial ovarian cancer. Global Medical Discovery Series (*Key Scientific Article Contributing to Excellence in Biomedical Research*), summer issue 2015.

3. *Fletcher NM, *Saed MG, Abu-Soud HM, Al-Hendy A, Diamond MP, **Saed GM**. Uterine fibroids are characterized by an impaired antioxidant cellular system: potential role of hypoxia in the pathophysiology of uterine fibroids. Featured article. MDLinx.com/ obstetrics-gynecology/ news-article, November 2013.

PRESENTATIONS

Podium Presentations (Referred)

1. *Novel Target for Ovarian Cancer Immunotherapy*. 48th Annual Meeting of the Society of Gynecologic Oncology's Women's Cancer, National Harbor, MD, March 2017.

2. *Targeting Integrin αV/β1 Receptor Manifests Intriguing Anti-Tumor Effects in Sensitive and Chemoresistant Ovarian Cancer Cells: Potential Therapeutic Target*. 64th Annual Scientific Meeting of the Society for Reproductive Investigation, Orlando, FL, March 2017.

3. *Human Adhesion Fibroblasts are Characterized by Reduction in the level* of *Pluripotency Markers as Compared to Normal Peritoneal Fibroblasts*. 72nd Annual Meeting of the American Society for Reproductive Medicine, Salt Lake City, UT, October 2016.

4. *Anti-Mullerian Hormone (AMH) for Prevention of Tissue Activation after Vitrified/Thawed Ovarian Cortex Xenotransplantation*. 72nd Annual Meeting of the American Society for Reproductive Medicine, Salt Lake City, UT, October 2016.

5. *Dichloroacetate Induces Apoptosis of Uterine Leiomyoma Cells Through A Mechanism Involving Modulation of Oxidative Stress*. 63rd Annual Meeting of the Society for Reproductive Investigation, Montreal, Quebec, Canada, March 2016.

6. *Chemoresistance in Epithelial Ovarian Cancer Cells is Controlled by Mechanisms Emanating from Chemotherapy-Induced Genotype Switch in Glutathione Peroxidase, Through the Up-Regulation of Cytidine Deminase*. 62nd Annual Meeting of the Society for Reproductive Investigation, San Francisco, CA, March 2015.

7. *Elevated Serum Anti-Müllerian Hormone (AMH) Stalls Ovarian Follicle Development by Downregulating FSH- and LH-Receptors and Inhibin-B Production*. Proceedings of the 71st Annual Meeting of the American Society for Reproductive Medicine, Baltimore, MD, October 2015.

8. *Hypochlorous Acid Reversibly Inhibits Caspase-3: A Potential Regulator of Apoptosis*. Joint Meeting of the 22nd Society for Redox Biology and Medicine (SFRBM) and 17th Society for Free Radical Research International (SFRRI), Boston, MA, November 2015.

9. *The In-Vivo Effects of Superoxide Dismutase on the Incidence and Severity of Post-Operative Adhesion Development*. 70th Annual Meeting of the American Society for Reproductive Medicine, Honolulu, HI, October 2014.

10. *Superoxide Dismutase Significantly Delayed the Development of Cisplatin Resistance in Epithelial Ovarian Cancer Cells*. American Association for Cancer Research's Precision Medicine Series: Drug Sensitivity and Resistance. Improving Cancer Therapy Special Conference, Orlando, FL, June 2014.

11. *Chemoresistant Ovarian Cancer Cells Manifest Lower Vascular Endothelial Growth Factor and Hypoxia Induced Factor-1α: A Potential Survival Mechanism*. American Association for Cancer Research's Precision Medicine Series: Drug Sensitivity and Resistance. Improving Cancer Therapy Special Conference, Orlando, FL, June 2014.

12. *Dicholoroacetate Increases Sensitivity to Chemotherapy by Modulation of Antioxidants in Epithelial Ovarian Cancer*. 61st Annual Meeting of the Society for Gynecologic Investigation, Florence, Italy, March 2014.

13. *Catalase and NADPH Oxidase Single Nucleotide Polymorphisms Are Associated with Increased Risk and Serve As Potential Targets for Breast and Ovarian Cancers*. 104th Annual Meeting of the American Association for Cancer Research, Washington, DC, April 2013.

14. *The Role of Oxidative Stress in the Development of Cisplatin Resistance in Epithelial Ovarian Cancer*. Poster session B. Advances in Ovarian Cancer Research: From Concept to Clinic. American Association for Cancer Research, Miami, FL, September 2013.

15. *Catalase and NADPH Oxidase Single Nucleotide Polymorphisms Are Associated with Increased Risk and Serve As Potential Targets for Breast and Ovarian Cancers*. 104th Annual Meeting of the American Association for Cancer Research, Washington, DC, April 2013.

16. *Endometrial Insulin Pathway during Ovarian Stimulation for Assisted Reproductive Technology (ART)*. 68th Annual Meeting of the American Society for Reproductive Medicine, San Diego, CA, October 2012.

17. *NADPH Oxidase p22-Phox Gene Polymorphism in Women is Associated with the Development of Postoperative Adhesions*. 59th Annual Meeting of the Society for Gynecologic Investigation, San Diego, CA, March 2012.

18. *Metabolism and Oxidative Stress: Integral Role in Regulation of the Adhesion Phenotype*. 58th Annual Meeting of the Society for Gynecologic Investigation, Miami Beach, FL, March 2011.

19. *Mass Spectrometric Identification of HOCl-Mediated Heme Degradation Products of Hemoglobin*. 59th ASMS Conference on Mass Spectrometry, Denver, CO, 2011.

20. *Inhibition of NADPH Oxidative Reductase Promotes Apoptosis in Epithelial Ovarian Cancer Cells*. 39th Annual Meeting of the Global Congress of Minimally Invasive Gynecology AAGL, Las Vegas, NV, November 2010.

21. *Reaction of Hemoglobin and Red Blood Cells with Hypochlorous Acid and Mechanism of Heme Destruction and Free Iron Release*. 17th Annual Meeting of the Society for Free Radical Biology and Medicine, Orlando, FL, November 2010.

22. *Liquid Chromatography Atmospheric Pressure Ionization Tandem: Mass Spectrometry Identifies Novel Hypochlorous Acid Reaction Products of Lycopene*. 58th Annual Meeting of the American Society of Mass Spectrometry, Salt Lake City, UT, May 2010.

23. *Role of Polychlorinated Biphenyls Enhancement of Lipid Peroxidation in Human Normal Peritoneal and Adhesion Fibroblasts*. 38th Annual Meeting of Global Congress of Minimally Invasive Gynecology AAGL, Orlando, FL, November 2009.

24. *Hydrogen Peroxide Bioavailability Determines the Sensitivity of Human Normal Peritoneal and Adhesion Fibroblasts to Hypoxia-Induced Lipid Peroxidation*. 38th Annual Meeting of Global Congress of Minimally Invasive Gynecology AAGL, Orlando, FL, November 2009.

25. *S-Nitrosylation of Caspase-3 Is the Mechanism by Which Adhesion Fibroblasts Manifest Lower Apoptosis*. 36th Annual Meeting of the American Association of Gynecologic Laparoscopists, Global Congress of Minimally Invasive Gynecology, Washington, DC, November 2007.

26. *Generation of Superoxide by Inducible Nitric Oxide Synthase in L-Arginine Deficient Fibroblasts Established From Human Adhesion Tissues*. 36th AAGL Annual Meeting, Global Congress of Minimally Invasive Gynecology, Washington, DC, November 2007.

27. *Hypoxia Stimulation of Expression of Type I Collagen and Fibronectin in Human Peritoneal and Adhesion Fibroblasts: Blockage by Interferon Gamma*. 36th AAGL Annual Meeting, Global Congress of Minimally Invasive Gynecology, Washington, DC, November 2007.

28. *Superoxide Induces the Adhesion Phenotype: Role of Hypoxia in the Pathogenesis of the Adhesion Development*. Global Congress of Minimally Invasive Gynecology, 36th Annual Meeting of the American Association of Gynecologic Laparoscopists, Washington, DC, November 2007.

29. *Nitric Oxide Synthase Isoforms are Differentially Expressed in Fibroblasts Isolated from Human Normal Peritoneum and Adhesion Tissues*. 63rd Annual Meeting of the American Society for Reproductive Medicine, Washington, DC, October 2007.

30. *Regulation of the Expression of INOS, COX-2, and VEGF in Postoperative Adhesions*. 62nd Annual Meeting of the American Society for Reproductive Medicine, New Orleans, LA, October 2006.

31. *Omega-3 Fatty Acid Prevents and Mitigates the Adhesion Phenotype in Normal Human Peritoneal and Adhesion Fibroblasts*. 62nd Annual Meeting of the American Society for Reproductive Medicine, New Orleans, LA, October 2006.

32. *IL6 Expression in Human Normal Peritoneal and Adhesion Fibroblasts: Regulation by Hypoxia*. 62nd Annual Meeting of the American Society for Reproductive Medicine, New Orleans, LA, October 2006.

33. *The Cross-Talk between Myeloperoxidase and Inducible Nitric Oxide Synthase in Post-operative Adhesions*. 62nd Annual Meeting of the American Society for Reproductive Medicine, New Orleans, LA, October 2006.

34. *TNF-Alpha Expression in Human Normal Peritoneal and Adhesion Fibroblasts: Regulation by Hypoxia*. 62nd Annual Meeting of the American Society for Reproductive Medicine, New Orleans, LA, October 2006.

35. *L-Arginine Deficiency in Fibroblasts Established from Human Adhesion Tissues Leads to the Generation of Superoxide by Inducible Nitric Oxide Synthase*. 53rd Annual Meeting of the Society for Gynecologic Investigation, Toronto, Ontario, Canada, March 2006.

36. *Regulation of Inducible Nitric Oxide Synthase in Post-Operative Adhesions*. 34th Annual Meeting of the American Association of Gynecologic Laparoscopists, Chicago, IL, November 2005.

37. *Cyclooxygenase-2 Inhibitors Enhance Apoptosis of Adhesion Fibroblasts*. 34th Annual Meeting of the American Association of Gynecologic Laparoscopists, Chicago, IL, November 2005.

38. *The Effects of Estradiol on the Expression of Estrogen, Progesterone, Androgen, and Prolactin Receptors in Human Peritoneal Fibroblasts*. 61st Annual Meeting of the American Society for Reproductive Medicine and the 1st Annual Meeting of the Canadian Fertility and Andrology Society, Palais des Congres, Montreal, Quebec, Canada, October 2005.

39. *Possible Role of Natural Immune Response against Fibroblasts in the Development of Post-Operative Adhesions*. 61st Annual Meeting of the American Society for Reproductive Medicine and the 51st Annual Meeting of the Canadian Fertility and Andrology Society, Palais des Congres, Montreal, Quebec, Canada, October 2005.

40. *Knockout of Inducible Nitric Oxide Expression Significantly Reduces the Expression of Type I Collagen and Transforming Growth Factor-β1 in Human Peritoneal and Adhesion Fibroblasts*. 61st Annual Meeting of the American Society for Reproductive Medicine and the 51st Annual Meeting of the Canadian Fertility and Andrology Society, Palais des Congres, Montreal, Quebec, Canada, October 2005. **Prize Paper Candidate**

41. *Regulation of Inducible Nitric Oxide Synthase in Post-Operative Adhesions*. 52nd Annual Meeting of the Society for Gynecologic Investigation, Los Angeles, CA, March 2005.

42. *Differential Expression of Myeloperoxidase (MPO) in Fibroblasts Isolated from Normal Peritoneal and Adhesion Tissues*. 4th International Peroxidase Meeting Joint with the 10th Myeloperoxidase Meeting, Shimokyo-Ku, Kyoto City, Japan, October 2004.

43. *Fibroblasts Isolated from Normal Peritoneal and Adhesion Tissues Differentially Express Myeloperoxidase (MPO)*. 60th Annual Meeting of the American Society for Reproductive Medicine, Philadelphia, PA, October 2004.

44. *Hypoxia Up-Regulates Cyclooxygenase-2 and Prostaglandin E_2 Levels in Human Peritoneal Fibroblasts*. 60th Annual Meeting of the American Society for Reproductive Medicine, Philadelphia, PA, October 2004.

45. *Dichloroacetate Inhibition of Angiogenesis Caused by Hypoxia Treatment of Normal Peritoneal and Adhesion Fibroblasts in Human Umbilical Vein Endothelial Cells*. 60th Annual Meeting of the American Society for Reproductive Medicine, Philadelphia, PA, October 2004.

46. *Dichloroacetate Significantly Increase the Expression of the Transcription Nuclear Factor Kappa-β in Fibroblasts of Human Adhesion Tissues*. 51st Annual Scientific Meeting of the Society for Gynecologic Investigation, Houston, TX, March 2004.

47. *Stimulation of Expression of Vascular Endothelial Growth Factor by Hypoxia from Fibroblasts Isolated from Normal Peritoneum and Adhesion Tissues*. 32nd Annual Meeting of The American Association of Gynecologic Laparoscopists, Las Vegas, NV, November 2003.

48. *Inhibition of Nitric Oxide Production by N-Nitro-L-Arginine Methyl Ester Increased the Expression of Type I Collagen in Human Peritoneal Fibroblasts*. 59th Annual Meeting of American Society for Reproductive Medicine, San Antonio, TX, October 2003.

49. *Apoptosis of Human Peritoneal and Adhesion Fibroblasts After Hypoxia: Role of Inducible Nitric Oxide Synthase*. 59th Annual Meeting of American Society for Reproductive Medicine, San Antonio, TX, October 2003.

50. *Inhibition of Cyclooxygenase-2 in Fibroblasts Isolated from Normal Peritoneum and Adhesion Tissues Decreases the Expression of Hypoxia Inducible Factor-1 Alpha*. 50th Annual Scientific Meeting of the Society for Gynecologic Investigation, Washington, DC, March 2003.

51. *Tissue Plasminogen Activator/Plasminogen Activator Inhibitor-1 (tPA/PAI-1) Modulation by Tisseel*. 50th Annual Scientific Meeting of the Society for Gynecologic Investigation, Washington, DC, March 2003.

52. *Hypoxia Increases the Expression of Vascular Endothelial Growth Factor in Fibroblasts Isolated From Human Normal Peritoneum and Adhesion Tissues*. 50th Annual Scientific Meeting of the Society for Gynecologic Investigation, Washington, DC, March 2003.

53. *Dichloroacetate Significantly Reduces the Expression of Vascular Endothelial Growth Factor in Fibroblasts of Human Adhesion Tissues*. 50th Annual Scientific Meeting of the Society for Gynecologic Investigation, Washington, DC, March 2003.

54. *Transforming Growth Factor-Beta 1 (TGF-β1) and Extracellular Matrix Production by Human Peritoneal Mesothelial Cells: Effect of Tisseel® Fibrin Sealant)*. 50th Annual Scientific Meeting of the Society for Gynecologic Investigation, Washington, DC, March 2003.

55. *Cyclooxygenase-2 Inhibition Decreases the Expression of Vascular Endothelial Growth Factor from Fibroblasts Isolated from Normal Peritoneum and Adhesion Tissues*. 50th Annual Scientific Meeting of the Society for Gynecologic Investigation, Washington, DC, March 2003.

56. *Elevation of Type I Collagen mRNA in Peritoneal Adhesions*. 31st Annual Meeting of the American Association of Gynecologic Laparoscopists, Miami, FL, November 2002.

57. *Cyclooxygenase-2 Expression in Human Fibroblasts Isolated from Adhesions But Not from Normal Peritoneal Tissues*. 31st Annual Meeting of the American Association of Gynecologic Laparoscopists, Miami, FL, November 2002.

58. *Existence of p53 Expression in Human Fibroblasts Isolated from Adhesions, But Not from Normal Peritoneal Tissues*. 31st Annual Meeting of the American Association of Gynecologic Laparoscopists, Miami, FL, November 2002.

59. *Matrix Metalloproteinase (MMP-1, MMP-2), and Tissue Inhibitor for Metalloproteinase (TIMP-1) Expression by Human Peritoneal Mesothelial Cells: Effect of Fibrin Sealant*. 58th Annual Meeting of the American Society for Reproductive Medicine, Seattle, WA, October 2002.

60. *Dichloroacetate (DCA) Significantly Increases the Expression of Inducible Nitric Oxide Synthase (INOS) in Human Fibroblasts of Adhesion Tissues, But Not In Normal Peritoneum*. 58th Annual Meeting of the Society for Reproductive Medicine, Seattle, WA, October 2002.

61. *Seprafilm (Modified Hyaluronic Acid Carboxymethylcellulose) Acts as a Mechanical Barrier*. 49th Scientific Meeting of the Society for Gynecologic Investigation, Los Angeles, CA, March 2002.

62. *Inhibition of Cyclooxygenase-2 in Human Adhesion Fibroblasts Reduces the Expression of MMP-1 and TIMP-1*. 49th Scientific Meeting of the Society for Gynecologic Investigation, Los Angeles, CA, March 2002.

63. *Inhibition of Cyclooxygenase-2 in Human Adhesion Fibroblasts Reduces the Expression of Transforming Growth Factor Beta-1*. 49th Scientific Meeting of the Society for Gynecologic Investigation, Los Angeles, CA, March 2002.

64. *Adhesion Phenotype: Cyclooxygenase-2 is Expressed in Fibroblasts Isolated From Adhesions, But Not From Normal Peritoneal Tissues*. 49th Scientific Meeting of the Society for Gynecologic Investigation, Los Angeles, CA, March 2002.

65. *Reduction of the Expression of Type I and III Collagens in Human Adhesion Fibroblasts, But Not in Normal Peritoneal Fibroblasts by the Inhibition of Cyclooxygenase-2*. 49th Scientific Meeting of the Society for Gynecologic Investigation, Los Angeles, CA, March 2002.

66. *Dichloroacetate Significantly Reduces the Expression of Cyclooxygenase-2 in Human Fibroblasts of Adhesion Tissues*. 49th Scientific Meeting of the Society for Gynecologic Investigation, Los Angeles, CA, March 2002.

67. *Adhesion Phenotype: p53 is Expressed in Fibroblasts Isolated From Adhesions But Not From Normal Peritoneal Tissues*. 49th Scientific Meeting of the Society for Gynecologic Investigation, Los Angeles, CA, March 2002.

68. *Metabolic Regulation of Collagen I in Fibroblasts Isolated from Normal Peritoneum and Adhesions by Dichloroacetic Acid (DCA)*. 28th Scientific Meeting of Gynecologic Surgeons, Dallas, TX, March 2002.

69. *An Adhesion Promoting Phenotype: Implications for Postoperative Adhesion Development*. 30th Annual Meeting American Association of Gynecologic Laparoscopists, Global Congress of Gynecologic Endoscopy, San Francisco, CA, November 2001.

70. *Differences in the Rate of Apoptosis Following Hypoxia in Human Peritoneal and Adhesion Fibroblasts*. 30th Annual Meeting American Association of Gynecologic Laparoscopists, Global Congress of Gynecologic Endoscopy, San Francisco, CA, November 2001.

71. *Modulation of the BCL-2/BAX Ratio by IFN-GAMMA and Hypoxia in Human Peritoneal and Adhesion Fibroblasts*. 57th Annual Meeting of the American Society for Reproductive Medicine, Orlando, FL, October 2001.

72. *Significance of the Effect of Hypoxia on the Rate of Apoptosis of Human Peritoneal and Adhesion Fibroblasts for Postoperative Adhesion Development*. 57th Annual Meeting of the American Society for Reproductive Medicine, Orlando, FL, October 2001.

73. *Prostaglandin E_2 Stimulates Proliferation and Reduces Apoptosis in Epithelial Ovarian Cancer Cell Lines*. 48th Annual Meeting of the Society for Gynecologic Investigation, Toronto, Canada, March 2001.

74. *Differential Modulation of BCL-2/BAX Ratio by Hypoxia in Peritoneal and Adhesion Fibroblasts Cultured from the Same Patient*. 48th Annual Meeting of the Society for Gynecologic Investigation, Toronto, Canada, March 2001.

75. *Interferon Gamma Blocks the Stimulating Effect of Hypoxia on the Expression of Type I Collagen and Fibronectin in Human Peritoneal and Adhesion Fibroblasts*. 48th Annual Meeting of the Society for Gynecologic Investigation, Toronto, Canada, March 2001.

76. *The Effect of Interferon Gamma and Hypoxia on the Expression of TGF-β Isoforms in Human Peritoneal and Adhesion Fibroblasts*. 48th Annual Meeting of the Society for Gynecologic Investigation, Toronto, Canada, March 2001.

77. *The Effect of Normoxia after Hypoxia Treatment of the Expression of Type I Collagen and TGF-β1 in Human Peritoneal Fibroblasts: Implications for Postoperative Adhesion Development*. 48th Annual Meeting of the Society for Gynecologic Investigation, Toronto, Canada, March 2001.

78. *Modulation of the BCL-2/BAX Ratio by IFN-γ and Hypoxia in Human Peritoneal and Adhesion Fibroblasts*. 32nd Annual Meeting of the Society of Gynecologic Oncologists, Nashville, TN, February 2001.

79. *Prostaglandin in Induced COX-2 Expression and Reduced Apopotosis in Epithelial Ovarian Cancer Cells*. 32nd Annual Meeting of the Society of Gynecologic Oncologists, Nashville, TN, February 2001.

80. *The Effect of Hypoxia on the Expression of HIF-1β, BAX, and BCL-2 in the Epithelial Ovarian Cancer Cell Line MADH2774*. 32nd Annual Meeting of the Society of Gynecologic Oncologists, Nashville, TN, February 2001.

81. *Induction of Cyclooxygenase-2 by Prostaglandin E_2 in Human Ovarian Cancer Cell Lines*. 53rd Congress of the DGGG, German Society of Gynecology and Obstetrics eV, Munich, Germany, June 2000.

82. *Type I Collagen Production by Human Peritoneal Fibroblasts in Response to Hypoxia and/or Transforming Growth Factor-Beta 1 (TGF-β1) Treatments*. 47th Annual Meeting of the Society for Gynecologic Investigation, SGI 2000-A Millennial Milestone in Reproductive Sciences: Celebrating the Promise, Chicago, IL, March 2000.

83. *The Effect of Hypoxia on TGF-β1 on the Expression of Cellular Fibronectin in Human Peritoneal Fibroblast Cells in Culture*. 47th Annual Meeting of the Society for Gynecologic Investigation, SGI 2000-A Millennial Milestone in Reproductive Sciences: Celebrating the Promise, Chicago, IL, March 2000.

84. *Type I Collagen Expression in Adhesion and Normal Peritoneal Tissues*. 47th Annual Meeting of the Society for Gynecologic Investigation, SGI 2000-A Millennial Milestone in Reproductive Sciences: Celebrating the Promise, Chicago, IL, March 2000.

85. *Vascular Endothelial Growth Factor (VEGF) Levels Are Elevated in Adhesion Tissue in Humans*. Annual Meeting of the American Association of Gynecologic Laparoscopists, Las Vegas, NV, November 1999.

86. *Basics of Cutaneous Wound Repair*. 4th International Conference on Postoperative Healing and Adhesions, Fort Lauderdale, FL, October 1999.

87. *The Role of Extracellular Matrix in the Formation of Postoperative Adhesion*. 4th International Conference on Postoperative Healing and Adhesions, Fort Lauderdale, FL, October 1999.

88. *The Effect of Hypoxia and TGF-β1 on the Expression of Tissue Inhibitors of Metalloproteinases (TIMP-1) in Human Peritoneal Mesothelial Cells*. Joint meeting of the Canadian Fertility Society and the American Society for Reproductive Medicine, Toronto, Ontario, Canada, September 1999.

89. *Collagen Type I and Type III Production by Human Mesothelial Cells in Response to Hypoxia and/or TGF-β1 Treatments*. Annual Meeting of the Society for Gynecologic Investigation, Atlanta, GA, March 1999.

90. *The Role of Apoptosis and p53 in the Pathogenesis of Keloids*. Journal of Investigative Dermatology 110: 597, 1998.

91. *Apoptosis Modulation in the Response of CTCL to PUVA*. Journal of Investigative Dermatology 110: 698, 1998.

92. *Apoptosis Dysregulation in Keloid Fibroblasts*. Journal of Investigative Dermatology 110:653, 1998.

93. *Apoptosis Regulation in the Pathogenesis of Cutaneous T-Cell Lymphoma (CTCL)*. Journal of Investigative Dermatology 108:610, 1997.

94. *The Effect of PUVA Treatment on HUT78 Cell Differential Gene Expression*. Journal of Investigative Dermatology 106:906, 1996.

95. *Detection of Differentially Displayed cDNA Fragments in Normal vs Sezary Syndrome Leukocytes*. Journal of Investigative Dermatology 104: 673, 1995.

96. *Quantitative PCR Analysis of Th-1 Cytokines in HUT78 Cells after Exposure to PUVA In Vitro*. Journal of Investigative Dermatology 102: 585, 1994.

97. *Augmentation of Th-1 Cytokines in the Peripheral Blood of Sezary Syndrome Patients after Treatment with ECCP*. Journal of Investigative Dermatology 102:586, 1994.

98. *Augmentation of Th-1 Cytokines in the Peripheral Blood of SZ Patients Upon Treatment with Extracorporeal Photopheresis*. Clinical Research 41:664, 1993.

99. *Detection of T-Cell Clonality in Mycosis Fungoides by PCR-Metaphore Agarose Analysis of T-Cell Receptor-γ*. Clinical Research 41:459, 1993.

100. *Mycosis Fungoides and Psoriasis Exhibit a Th1 Type Cell Mediated Response While Sezary Syndrome Expresses A Th2 Type Response*. Clinical Research 40:730, 1992.

101. *T-Cell Receptor Gene Conservation and Rearranged Clones in Canine Mycosis Fungoides*. Clinical Research 40:505, 1992.

Poster Presentations (Referred)

1. Fletcher NM, Awonuga AO, Memaj I, Diamond MP, **Saed GM**. Interruption of MPO Binding to CD11B Selectively Kills Fibroblasts from Adhesion Tissues but not Normal Peritoneum. 73rd American Society for Reproductive Medicine Scientific Congress & Expo, San Antonio, TX, October-November 2017. Proceedings: P-264, 216, 2017. **SRS In-Training Award for Research to NM Fletcher, PhD**

2. Fletcher NM, Memaj I, Abusamaan MS, Juhani A, Al-Hendy A, Diamond MP, **Saed GM**. Oxidative Stress: A Key Regulator of Leiomyoma Cell Survival. 64th Annual Scientific Meeting for the Society for Reproductive Investigation, Orlando, FL, March 2017. Fertility and Sterility 24(1) Supplement: F-124, 208A, 2017.

3. Detti L, Fletcher NM, **Saed GM**, Uhlmann RA, Christiansen ME, Williams LJ. Anti-Mullerian Hormone (AMH) Regulates BRCA1 and BRCA2 Gene Expression in an Ovarian Cortex Transplantation Model. 72nd Annual Meeting of the American Society for Reproductive Medicine, Salt Lake City, UT, October 2016. Fertility and Sterility 106(3) Supplement: P-037, e120, 2016.

4. Fletcher NM, Belotte J, Saed MG, Abusamaan MS, Diamond MP, **Saed GM**. Chemotherapy Induces a Genotype Switch in Key Antioxidant Enzymes: A Potential Mechanism of Chemoresistance in Epithelial Ovarian Cancer Cells. 63rd Annual Meeting of the Society for Reproductive Investigation, Montreal, Quebec, Canada, March 2016. Reproductive Sciences 23(1) Supplement: F-248, 262-263A, 2016.

5. Detti L, Fletcher NM, Uhlmann RA, Belotte J, Williams LJ, **Saed GM**. Exposure to Recombinant Anti-Mullerian Hormone (AMH) Downregulates Ovarian Follicle Cells' Stemness Potential in Fresh and Vitrified/Thaw Ovarian Cortex. 63rd Annual Meeting of the Society for Reproductive Investigation, Montreal, Quebec, Canada, March 16-19, 2016. Reproductive Sciences 23(1) Supplement: T-257, 180A, 2016.

6. Nusrat O, Belotte J, Fletcher NM, Saed MG, Diamond MP, **Saed GM**. Chemoresistant Ovarian Cancer Cells Manifest Lower Vascular Endothelial Growth Factor and Hypoxia Inducible Factor-1α: A Potential Survival Mechanism. 63rd Annual Meeting of the Society for Reproductive Investigation, Montreal, Quebec, Canada, March 16-19, 2016. Reproductive Sciences 23(1) Supplement: T-250, 178A, 2016.

7. Fletcher NM, Neubauer BR, Saed MG, Abu-Soud HM, **Saed GM**. 2,4-Dinitrophenol Induced Cell Death of Ovarian Cancer Stem Cells. 62nd Annual Meeting of the Society for Reproductive Investigation, San Francisco, CA, March 2015. Reproductive Sciences 22(1) Supplement: S-003, 299A, 2015.

8. Fletcher NM, Neubauer BR, Saed MG, Diamond MP, Abu-Soud HM, **Saed GM**. Postoperative Adhesion Development is Controlled by Mechanisms Emanating from a Hypoxia-Induced Genotype Switch in Nicotinamide Adenine Dinucleotide Phosphate Oxidase Through the Up-Regulation of Cytidine Deaminase. 62nd Annual Meeting of the Society for Reproductive Investigation, San Francisco, CA, March 2015. Reproductive Sciences 22(1) Supplement: F-042, 218A, 2015.

9. Detti L, Williams LJ, Fletcher NM, **Saed GM**. Anti-Müllerian Hormone (AMH) May Inhibit Oocyte Maturation and Follicular Vascularization in Human Ovarian Cortex. Proceedings of the 71st Annual Meeting of the American Society for Reproductive Medicine, Baltimore, MD, October 2015. Fertility and Sterility 104(3) Supplement: P91, e136, 2015.

10. Fletcher NM, Saed MG, Neubauer BR, Abusamaan MS, Al-Hendy A, Diamond MP, Berman JM, **Saed GM**. Uterine Fibroids Are Characterized by An Altered Redox Balance, Favoring A Pro-Oxidant State. 71st Annual Meeting of the American Society for Reproductive Medicine, Baltimore, MD, October 2015. Fertility and Sterility 104(3) Supplement: P-115, e145, 2015.

11. Fletcher NM, Saed MG, Neubauer BR, Abu-Soud HM, Awonuga A, Diamond MP, **Saed GM**. Shifting Anaerobic to Aerobic Metabolism Stimulates Apoptosis in Adhesion Fibroblasts Through the Modulation of the Cellular Redox Homeostasis. 71st Annual Meeting of the American Society for Reproductive Medicine, Baltimore, MD, October 2015. Fertility and Sterility 104(3) Supplement: P-215, e179, 2015.

12. Abusamaan MS, Fletcher NM, Saed MG, Al-Hendy A, Diamond MP, Berman JM, **Saed GM**. Myeloperoxidase Serves As A Redox Switch That Regulates Apoptosis In Human Leiomyomas. 71st Annual Meeting of the American Society for Reproductive Medicine, Baltimore, MD, October 2015. Fertility and Sterility 104(3) Supplement: P-113, e145, 2015.

13. Fletcher NM, Detti L, Neubauer BR, Saed MG, Diamond MP, Abuzeid MI, **Saed GM**. Altered Redox State in the Endometrium of Patients Undergoing Ovarian Stimulation for Assisted Reproduction Technology. Proceedings of the 70th Annual Meeting of the American Society for Reproductive Medicine, Honolulu, HI, October 2014. Fertility and Sterility 102(35) Supplement: P-426, e279, 2014.

14. Belotte J, Fletcher NM, Diamond MP, **Saed GM**. Sox2 Gene Amplification Impacts Survival in Serous Epithelial Ovarian Cancer. 61st Annual Meeting of the Society for Investigation, Florence, Italy, March 2014. Reproductive Sciences 21(3) Supplement: T-219, 204A, 2014.

15. **Saed GM**, Fletcher NM, Belotte J, Levin NK, Simon MS, Abu-Soud HM, Tainsky MA, Diamond. SNPs in Key Oxidants and Antioxidants Are Associated with Increased Risk and Serve as Potential Targets for Ovarian Cancer. 61st Annual Meeting of the Society for Gynecologic Investigation, Florence, Italy, March 2014. Reproductive Sciences 21(3) Supplement: T-249, 213A, 2014.

16. Diamond MP, Fletcher NM, Saed MG, Abu-Soud HM, Al-Hendy A, **Saed GM**. Fibroids Manifest Oxidative Stress As Compared to Normal Myometrium. 42nd Annual AAGL Global Congress of Minimally Invasive Gynecology, Washington, DC, November 2013. The Journal of Minimally Invasive Gynecology 20(6) Suppl: S19, 2013.

17. Diamond MP, Fletcher NM, Abuanzeh S, Saed MG, **Saed GM**. Creation and Persistence of the Adhesion Phenotype: The Role of NOXs in Creating Oxidative Stress. 42nd Annual AAGL Global Congress of Minimally Invasive Gynecology, Washington, DC, November 2013.

18. Fletcher NM, Saed MG, Abu-Soud HM, Al-Hendy A, Diamond MP, **Saed GM**. Distinct Oxidative Stress Profile in Uterine Fibroids Versus Adjacent Myometrium. Conjoint Meeting of the International Federation of Fertility Societies and the 69th American Society for Reproductive Medicine, Boston, MA, October 2013. Fertility and Sterility 100(3) Suppl: S34, 2013.

19. Fletcher NM, Abuanzeh S, Saed MG, Abu-Soud HM, Diamond MP, **Saed GM**. Postoperative Adhesion is Characterized by a Unique Oxidative Stress Profile Which is Responsible for Creation and Persistence of the Adhesion Phenotype. Conjoint Meeting of the International Federation of Fertility Societies and the 69th American Society for Reproductive Medicine, Boston, MA, October 2013. Fertility and Sterility 100(3) Suppl: S31, 2013.

20. Thakur M, Imudia AN, Shavell VI, Singh M, Diamond MP, Awonuga AO, **Saed GM**. Should Body Mass Index Influence the Dose of hCG for Ovulation Induction After Superovulation in IVF/ICSI cycles? 68th Annual Meeting of the American Society for Reproductive Medicine, San Diego, CA, October 2012. Fertility and Sterility 98(3) Suppl: P-542, S271, 2012.

21. Fletcher NM, Al-Hendy A, Diamond M, **Saed GM**. Uterine Fibroids Are Characterized by an Impaired Antioxidant Cellular System: Potential Role of Hypoxia in the Pathophysiology of Fibroids. 68th Annual Meeting of the American Society for Reproductive Medicine, San Diego, CA, October 2012. Fertility and Sterility 98(3) Suppl: P-403, S231, 2012.

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127. Fivenson DP, **Saed GM**, Nickoloff BJ. Modulation of IL-10 expression in HUT78 cells: insights into the pathobiology and treatment of CTCL. Clinical Research 42: 232, 1994.

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Other

1. **Saed GM**, Fletcher NM, Memaj I. Abciximab manifests striking anti-tumor effects in sensitive and chemoresistant ovarian cancer cells. Joint Annual Reproductive Sciences Retreat, Departments of Obstetrics and Gynecology, Wayne State University School of Medicine and The University of Toronto; and Annual Michigan Alliance for Reproductive Technologies and Sciences Meeting at Wayne State University, Detroit, MI, October 2017. Proceedings: A-02, pg. 2, 2017.

2. Nusrat O, Fletcher NM, Belotte J, Saed MG, Neubauer BR, **Saed GM**. Chemoresistant ovarian cancer cells manifest lower vascular endothelial growth factor and hypoxia inducible factor-1α: a potential survival mechanism. Integrative Global Approaches in Reproductive Sciences. 6th Annual C.S. Mott Center for Human Growth and Development & Lunenfeld-Tanenbaum Research Institute Joint Scientific Retreat, Wayne State University School of Medicine and University of Toronto, Detroit, MI, April 2015. Proceedings: A-48, pg. 49, 2015.

3. Fletcher NM, Neubauer BR, Saed MG, Abu-Soud HM, **Saed GM**. Chemoresistance in epithelial ovarian cancer cells is controlled by mechanisms emanating from chemotherapy-induced genotype switch in oxidant and antioxidant enzymes, through the upregulation of cytidine deaminase. Integrative Global Approaches in Reproductive Sciences. 6th Annual C.S. Mott Center for Human Growth and Development & Lunenfeld-Tanenbaum Research Institute Joint Scientific Retreat, Wayne State University School of Medicine and University of Toronto, Detroit, MI, April 2015. Proceedings and Abstracts: A-47, pg. 48, 2015.

4. Khan SN, Shaeib FN, Najafi T, **Saed G**, Abu-Soud HM. Diffused intra-oocyte hydrogen peroxide activates myeloperoxidase and deteriorates oocyte quality. 6th Annual C.S. Mott Center for Human Growth and Development & Lunenfeld-Tanenbaum Research Institute Joint Scientific Retreat, Wayne State University School of Medicine and University of Toronto, Detroit, MI, April 2015. Proceedings and Abstracts: A-13, pg. 14, 2015.

5. Shaeib F, Khan SN, **Saed G**, Abu-Soud HM. Macrophages activation deteriorates metaphase II mouse oocyte through myeloperoxidase action. Integrative Global Approaches in Reproductive Sciences. 6th Annual C.S. Mott Center for Human Growth and Development & Lunenfeld-Tanenbaum Research Institute Joint Scientific Retreat, Wayne State University School of Medicine and University of Toronto, Detroit, MI, April 2015. Proceedings and Abstracts: A-18, pg. 19, 2015.

6. Jeelani R, Sliskovic I, **Saed G**, Pennathur S, Abu-Soud HM. Hypochlorous acid reversibly inhibits caspase-3: a potential regulator of apoptosis. Integrative Global Approaches in Reproductive Sciences. 6th Annual C.S. Mott Center for Human Growth and Development & Lunenfeld-Tanenbaum Research Institute Joint Scientific Retreat, Wayne State University School of Medicine and University of Toronto, Detroit, MI, April 2015. Proceedings and Abstracts: A-16, pg. 17, 2015.

7. Shaeib F, Khan SN, Ali I, Dai J, Drewlo S, **Saed GM**, Abu-Soud HM. The impact of myeloperoxidase on metaphase II mouse oocyte quality. Proceedings of the Graduate Research Day, Wayne Day 2014 Program, Current Concepts in Gynecologic Oncology for the Obstetrician and Gynecologist, Kamran S. Moghissi, M.D. Lecture, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI, December 2014.

8. Fletcher NM, Belotte J, Saed MG, Abu-Soud HM, Diamond MP, **Saed GM**. Dicholoroacetate increases sensitivity to chemotherapy by modulation of antioxidants in epithelial ovarian cancer. Proceedings of the Graduate Research Day, Wayne Day 2014 Program, Current Concepts in Gynecologic Oncology for the Obstetrician and Gynecologist, Kamran S. Moghissi, M.D. Lecture, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI, December 2014.

9. Shaeib F, Khan SN, Banerjee J, Thakur M, Dai J, Awonuga AO, **Saed GM**, Abu-Soud HM. Role of cumulus cells in defense against reactive oxygen species insult in metaphase II mouse oocytes. 4th Annual Scientific Retreat of The C.S. Mott Center for Human Growth and Development, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI, May 2014. Program and Abstracts: #P-26, pg. 39, 2014.

10. Nusrat O, Fletcher NM, Belotte J, Saed MG, Neubauer BR, **Saed GM**. Chemoresistant ovarian cancer cells manifest lower vascular endothelial growth factor and hypoxia induced factor-1α: a potential survival mechanism. 4th Annual Scientific Retreat of The C.S. Mott Center for Human Growth and Development, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI, May 2014. Program and Abstracts: #P-23, pg. 36, 2014.

11. Najafi T, Goud PT, Goud AP, Gonik B, **Saed GM**, Zhang X, Abu-Soud HM. Direct real-time measurement of intra-oocyte nitric oxide concentration *in vivo*. 4th Annual Scientific Retreat of The C.S. Mott Center for Human Growth and Development, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI, May 2014; Program and Abstracts: #P-22, pg. 35, 2014.

12. Fletcher NM, Belotte J, Saed MG, Abu-Soud HM, Diamond MP, **Saed GM**. Dicholoroacetate increases sensitivity to chemotherapy by modulation of antioxidants in epithelial ovarian cancer. 4th Annual Scientific Retreat of The C.S. Mott Center for Human Growth and Development, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI, May 2014. Program and Abstracts: #P-07, pg. 20, 2014.

13. Belotte J, Fletcher NM, Saed MG, Neubauer BR, **Saed GM**. RAD21 gene amplification impacts survival in serous epithelial ovarian cancer. 4th Annual Scientific Retreat of The C.S. Mott Center for Human Growth and Development, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI, May 2014. Program and Abstracts: #P-04, pg. 17, 2014.

14. Belotte J, Fletcher NM, Nusrat O, Saed MG, Neubauer BR, Abu-Soud HM, **Saed GM**. Superoxide dismutase significantly delayed the development of cisplatin resistance in epithelial ovarian cancer cells. 4th Annual Scientific Retreat of The C.S. Mott Center for Human Growth and Development, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI, May 2014. Program and Abstracts: #P-03, pg. 16, 2014.

15. Awonuga AO, Fletcher NM, Belotte J, Diamond MP, **Saed GM**. The in-vivo effects of superoxide dismutase on the incidence and severity of postoperative adhesion development. 4th Annual Scientific Retreat of The C.S. Mott Center for Human Growth and Development, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI, May 2014. Program and Abstracts: #P-02, pg. 15, 2014.

16. **Saed GM**. The role of oxidative stress in the pathogenesis of pro-fibrotic gynecologic disorders. 4th Annual Scientific Retreat of The C.S. Mott Center for Human Growth and Development, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI, May 2014. Program and Abstracts: #O-13, pg. 13, 2014.

17. Najafi T, Goud AP, Goud PT, **Saed GM**, Gonik B, Abu-Soud HM. Release of substrates, cofactors, and products of nitric oxide synthase are altered during oocyte aging. 4th Annual Scientific Retreat of The C.S. Mott Center for Human Growth and Development, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI, May 2014. Program and Abstracts: #O-12, pg. 12, 2014.

18. Shaeib F, Khan SN, Ali I, Dai J, Drewlo S, **Saed GM**, Abu-Soud HM. The impact of myeloperoxidase on metaphase II mouse oocyte quality. 4th Annual Scientific Retreat of The C.S. Mott Center for Human Growth and Development, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI, May 2014. Program and Abstracts: #O-11, pg. 11, 2014.

19. Fletcher NM, **Saed GM**. Differential expression of glutathione peroxidase and glutathione reductase in chemoresistant epithelial ovarian cancer cells. 4th Annual Research Symposium of the Michigan Alliance for Reproductive Technologies and Science (MARTS), University of Michigan, Ann Arbor, MI, May 2013.

20. Shaeib F, Banerjee J, Thakur M, Saed MG, Diamond MP, **Saed GM**, Abu-Soud HM. Confocal 3-dimensional reconstruction can serve as a useful tool to quantify oxidative stress induced oocyte spindle damage. 3rd Annual Scientific Retreat of The C.S. Mott Center for Human Growth and Development, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI, May 15, 2013. Program and Abstracts: #35, 2013.

21. Fletcher NM, **Saed GM**. Differential expression of glutathione peroxidase and glutathione reductase in chemoresistant epithelial ovarian cancer cells. 3rd Annual Scientific Retreat of The C.S. Mott Center for Human Growth and Development, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI, May 2013: Program and Abstracts: #26, 2013.

22. **Saed GM**. Investigation of the role of oxidative stress in the pathophysiology of gynecologic fibrotic disorders including postoperative adhesions, fibroids, and endometriosis as well as ovarian cancer. 3rd Annual Scientific Retreat of The C.S. Mott Center for Human Growth and Development, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI, May 2013. Program and Abstracts: #20, 2013.

23. Belotte J, Mitchell A, Belotte J, **Saed GM**. Sox2 gene copy number alteration (CAN) significantly impact overall survival (OS) in serous epithelial ovarian cancer. 3rd Annual Scientific Retreat of The C.S. Mott Center for Human Growth and Development, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI, May 2013. Program and Abstracts: #6, 2013.

24. Belotte J, Fletcher NM, Abuanzeh S, Levin NK, Simon NS, Diamond MP, Abu-Soud HM, Tainsky MA, **Saed GM**. A novel association between a catalase single nucleotide polymorphism and increased risk of ovarian cancer. 3rd Annual Scientific Retreat of The C.S. Mott Center for Human Growth and Development, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI, May 2013. Program and Abstracts: #4, 2013.

25. Awonuga AO, King NM, Belotte J, Abuanzeh S, Diamond MP, **Saed GM**. The in vitro effects of superoxide dismutase on the incidence and severity of post-operative adhesion development after cecal abrasion. 3rd Annual Scientific Retreat of The C.S. Mott Center for Human Growth and Development, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI, May 2013. Program and Abstracts: #3, 2013.

26. Shavell VI, Fletcher NM, Abu-Soud HM, Diamond MP, **Saed GM**, Detti L. Superoxide dismutase levels are elevated in the peri-implantation endometrium in women undergoing ovarian stimulation. 3rd Annual Michigan Alliance for Reproductive Technologies and Science Research Symposium, Wayne State University School of Medicine, Detroit, MI, May 2012. Proceedings and Abstracts: #15, 2012.

27. Maitra D, Abdulhamid I, **Saed GM**, Diamond MP, Pennathur S, Abu-Soud HM. Fluorescent heme degradation products in Sickle cell disease: role of hypochlorous acid in hemoglobin destruction. 3rd Annual Michigan Alliance for Reproductive Technologies and Science Research Symposium, Wayne State University School of Medicine, Detroit, MI, May 2012. Proceedings and Abstracts: #12, 2012.

28. Maitra D, Abdulridha RM, Byun J, Souza CEA, Banerjee J, Andreana PR, Diamond MP, **Saed GM**, Pennathur S, Abu-Soud. The reaction of HOCl and cyanocobalamin: corrin destruction and the liberation of cyanogens chloride. 3rd Annual Michigan Alliance for Reproductive Technologies and Science Research Symposium, Wayne State University School of Medicine, Detroit, MI, May 2012. Program and Abstracts: #11, 2012.

29. Fletcher NM, Belotte J, Diamond MP, **Saed GM**. Dicholoroacetate increases sensitivity to chemotherapy treatment of epithelial ovarian cancer cells. 3rd Annual Michigan Alliance for Reproductive Technologies and Science Research Symposium, Wayne State University School of Medicine, Detroit, MI, May 2012. Program and Abstracts: #8, 2012.

30. Belotte J, Fletcher NM, Diamond MP, **Saed GM**. The role of oxidative stress in the development of cisplatin resistance in epithelial ovarian cancer. 3rd Annual Michigan Alliance for Reproductive Technologies and Science Research Symposium, Wayne State University School of Medicine, Detroit, MI, May 2012. Program and Abstracts: #6, 2012.

31. Banerjee J, Maitra D, Shaeib F, **Saed GM**, Diamond MP, Abu-Soud HM. Melatonin prevents hypochlorous acid induced alteration of the metaphase-II mouse oocyte microtubule and chromosomal structure. 3rd Annual Michigan Alliance for Reproductive Technologies and Science Research Symposium, Wayne State University School of Medicine, Detroit, MI, May 2012. Program and Abstracts: #5, 2012.

32. Maitra D, Shaeib F, Abdulridha RM, Souza CEA, **Saed GM**, Abu-Soud HM. Modulation of myeloperoxidase activity by self-generated hypochlorous acid. 3rd Annual Michigan Alliance for Reproductive Technologies and Science Research Symposium, Wayne State University School of Medicine, Detroit, MI, May 2012. Program and Abstracts: #1, 2012.

33. Maitra D, Shaeib F, Abdulridha RM, Souza CEA, **Saed GM**, Abu-Soud HM. Modulation of myeloperoxidase activity by self-generated hypochlorous acid. 2nd Annual Scientific Retreat of The C.S. Mott Center for Human Growth and Development, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI, May 2012. Program and Abstracts: #32, 2012.

34. Fletcher NM, Belotte J, Diamond MP, **Saed GM**. Dicholoroacetate increases sensitivity to chemotherapy treatment of epithelial ovarian cancer cells. 2nd Annual Scientific Retreat of The C.S. Mott Center for Human Growth and Development, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI, May 2012. Program and Abstracts: #31, 2012.

35. Belotte J, Fletcher NM, Diamond MP, **Saed GM**. The role of oxidative stress in the development of cisplatin resistance in epithelial ovarian cancer. 2nd Annual Scientific Retreat of The C.S. Mott Center for Human Growth and Development, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI, May 2012. Program and Abstracts: #29, 2012.

36. Banerjee J, Maitra D, Shaeib F, **Saed GM**, Diamond MP, Abu-Soud HM. Melatonin prevents hypochlorous acid induced alteration of the metaphase-II mouse oocyte microtubule and chromosomal structure. 2nd Annual Scientific Retreat of The C.S. Mott Center for Human Growth and Development, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI, May 2012. Program and Abstracts: #25, 2012.

37. Maitra D, Abdulridha RM, Byun J, Souza CEA, Banerjee J, Andreana PR, Diamond MP, **Saed GM**, Pennathur S, Abu-Soud HM. The reaction of HoCl and cyanocobalamin: corrin destruction and the liberation of cyanogens chloride. 2nd Annual Scientific Retreat of The C.S. Mott Center for Human Growth and Development, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI, May 2012. Program and Abstracts: #23, 2012.

38. Shavell VI, Fletcher NM, Abu-Soud HM, Diamond MP, **Saed GM**, Detti LL. Superoxide dismutase levels are elevated in the peri-implantation endometrium in women undergoing ovarian stimulation. 2nd Annual Scientific Retreat of The C.S. Mott Center for Human Growth and Development, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI, May 2012. Programs and Abstracts: #17, 2012.

39. Maitra D, Abdulhamid I, **Saed GM**, Diamond MP, Pennathur S, Abu-Soud HM. Fluorescent heme degradation products in sickle cell disease: role of hypochlorous acid in hemoglobin destruction. 2nd Annual Scientific Retreat of The C.S. Mott Center for Human Growth and Development, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI, May 2012. Programs and Abstracts: #16, 2012.

40. **Saed GM**. Investigation of the role of oxidative stress in the pathophysiology of gynecologic fibrotic disorders including postoperative adhesions, fibroids, and endometriosis as well as ovarian cancer. 2nd Annual Scientific Retreat of The C.S. Mott Center for Human Growth and Development, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI, May 2012. Program and Abstracts: #9, 2012.

41. Shavell VI, Fletcher NM, Jiang ZL, **Saed GM**, Diamond MP. Coupling oxidative phosphorylation with 2,4-dinitrophenol promotes development of the adhesion phenotype. 1st Annual Scientific Retreat of The C.S. Mott Center for Human Growth and Development, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Southfield, MI, May 2011. Program and Abstracts: #26, 2011.

42. **Saed GM**. The role of oxidative stress in the pathophysiology of gynecologic fibrotic disorders including postoperative adhesions, fibroids, and endometriosis, as well as ovarian cancer. 1st Annual Scientific Retreat of The C.S. Mott Center for Human Growth and Development, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Southfield, MI, May 2011. Program and Abstracts: #24, 2011.

43. Maitra D, Shaeib F, Diamond MP, **Saed GM**, Abu-Soud HM. Melatonin can attenuate HOCl mediated hemolysis, free iron release and heme degradation from hemoglobin. 1st Annual Scientific Retreat of The C.S. Mott Center for Human Growth and Development, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Southfield, MI, May 2011. Program and Abstracts: #19, 2011.

44. Maitra D, Byun J, Andreana PR, Abdulhamid I, Diamond MP, **Saed GM**, Pennathur S, Abu-Soud HM. Reaction of hemoglobin with HOCl: possible link between free iron accumulation and oxidative stress. 1st Annual Scientific Retreat of The C.S. Mott Center for Human Growth and Development, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Southfield, MI, May 2011. Program and Abstracts: #18, 2011.

45. Fletcher NM, Jiang ZL, Levin NK, Abu-Soud HM, Munkarah AR, Tainsky MA, Diamond MP, **Saed GM**. Positive correlation between serum myeloperoxidase and free iron levels with stage of ovarian cancer: potential biomarkers for early detection and prognosis of ovarian cancer. 1st Annual Scientific Retreat of The C.S. Mott Center for Human Growth and Development, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Southfield, MI, May 2011. Program and Abstracts: #13, 2011.

46. Banerjee J, Maitra D, Shaeib F, **Saed GM**, Diamond MP, Abu-Soud HM. Role of melatonin in preventing hypochlorous acid induced alterations in microtubule and chromosomal structure in metaphase-II mouse oocytes *in vitro*. 1st Annual Scientific Retreat of The C.S. Mott Center for Human Growth and Development, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Southfield, MI, May 2011. Program and Abstracts: #7, 2011.

47. Diamond MP, **Saed GM**. Reduction of postoperative adhesions. Catalyzing Collaboration between Industry and Academic in the Life Sciences – Women's Health Medicine: Part I, Therapeutic Strategies Meeting, Illinois Science and Technology Park, Skokie, IL, June 2007. Proceedings 2007.

Invited Lectures/Presentations

International/National

1. *Targeting Integrin αV/β1 Receptor Manifests Intriguing Anti-Tumor Effects in Sensitive and Chemoresistant Ovarian Cancer Cells: Potential Therapeutic Target*. 64th Annual Scientific Meeting of the Society for Reproductive Investigation, Orlando, FL, March 2017.

2. *The Role of Oxidative Stress in the Pathogenesis of Ovarian Cancer*. University of Jordan, Amman, Jordan, July 2017.

3. *Novel Innovative Targets for Ovarian Cancer Therapy*. King Hussein Cancer Center, Amman, Jordan, July 2017.

4. *The Role of Oxidative Stress in the Pathogenesis of Ovarian Cancer*. King Hussein Cancer Center, Amman, Jordan, November 2016.

5. *The Role of Oxidative Stress in the Pathogenesis of Ovarian Cancer*. University of Jordan, Amman, Jordan, November 2016.

6. *New Insights for Ovarian Cancer Screening*. 4th International Conference of the Jordanian Society of Pathology and Laboratory Medicine. In collaboration with the Arabic Division of the International Academy of Pathology, Amman, Jordan, April 2011.

7. *Updates in Oxidative Stress and Ovarian Cancer*. Modern Technology Application in Pathology Conference, Amman, Jordan, July 22 – August 1, 2010.

8. *The Role of p53 in the Pathogenesis of Keloids*. International Meeting on Mechanisms Involved in Tissue Repair and Fibrosis: Role of the Microfibroblast (Differentiation and Apoptosis), Lyon, France, December 1997.

Local/Regional

1. *The Role of Oxidative Stress in the Pathogenesis of Ovarian Cancer*. Joint Annual Reproductive Sciences Retreat, Departments of Obstetrics and Gynecology, Wayne State University School of Medicine and The University of Toronto; and Annual Michigan Alliance for Reproductive Technologies and Sciences (MARTS) Meeting at Wayne State University, Detroit, MI, October 2017. Retreat

2. *Invited Guest Speaker*. Tumor Microenvironment Section, Karmanos Cancer Center, Detroit Medical Center/Wayne State University School of Medicine, Detroit, MI, June 2016.

3. *Molecular Biological Procedures*. C.S. Mott Center for Human Growth and Development, Division of Reproductive Endocrinology and Infertility Laboratory Techniques Summer Course, Wayne State University School of Medicine, Detroit, MI, September 2015.

4. *New Insights into Pathogenesis of Ovarian Cancer*. The C.S. Mott Center Summer Reproductive Sciences Technology Course, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI, July 2014.

5. *The Role of Oxidative Stress in the Pathogenesis of Pro-Fibrotic Gynecologic Disorders*. 4th Annual Scientific Retreat, The C.S Mott Center for Human Growth and Development, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI, May 2014.

6. *Release of Substrates, Cofactors, and Products of Nitric Oxide Synthase Are Altered during Oocyte Aging*. 4th Annual Scientific Retreat, The C.S Mott Center for Human Growth and Development, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI, May 2014.

7. *The Impact of Myeloperoxidase on Metaphase II Mouse Oocyte Quality*. 4th Annual Scientific Retreat, The C.S Mott Center for Human Growth and Development, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI, May 2014. **First Prize Award**

8. *Differential Expression of Glutathione Peroxidase and Glutathione Reductase in Chemoresistant Epithelial Ovarian Cancer Cells*. The Michigan Alliance for Reproductive Technologies and Science (MARTS), Fourth Annual Research Symposium, University of Michigan, Ann Arbor, MI, May 2013.

9. *The Role of Oxidative Stress in the Pathophysiology of Gynecologic Fibrotic Disorders: Postoperative Adhesions, Fibroids, Endometriosis, and Ovarian Cancer*. 1st Annual Scientific Retreat of The C.S. Mott Center for Human Growth and Development, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Southfield, MI, May 2011.

10. *New Insights in Ovarian Cancer Screening*. Department of Obstetrics and Gynecology Wayne Day: New Frontiers in the Treatment of Gynecologic Cancer, Wayne State University School of Medicine, Detroit, MI, December 2010.

11. *Molecular Characterization of Adhesion and Peritoneal Fibroblasts*. Adhesion Mini Symposium, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI, March 2001.

12. *Multiplex RT/PCR Technique, Concept and Application*. Center for Biomedical Research, College of Art and Sciences, Oakland University, Rochester, MI, May 1999.

13. *Techniques for Characterizing and Manipulating DNA from the Basis of Much of Modern Biomedical Research*. Department of Chemistry, Oakland University, Rochester, MI, January 1999.

14. *Bcl-2/Bax Ratio as a Measure of the Rate of Apoptosis in Keloid Fibroblasts*. Oxford Biomedical Research Inc., Oxford, MI, January 1998.

15. *PCR Techniques, Concepts and Applications*. Howard Hughes Research Program, Oakland University, Rochester, MI, May 1998.

16. *Multiplex RT/PCR Technique, Concept and Application*. Center for Biomedical Research, College of Art and Sciences, Oakland University, Rochester, MI, May 1997.

17. *Application of RT/PCR*. Department of Chemistry, Oakland University, Rochester, MI, June 1994.

Invited Seminars and Grand Rounds

1. *New Insights into the Pathogenesis of Post-Operative Adhesions Development*. Department of Obstetrics and Gynecology Grand Rounds, Georgia Regents University, Augusta, GA, January 2017.

2. *Novel Innovative Targets for Ovarian Cancer Therapy*. Cancer Center Seminar, Georgia Regents University, Augusta, GA, January 2017.

3. *The Role of Oxidative Stress in the Pathogenesis of Pro-Fibrotic Gynecologic Disorders*. Augusta Research Day, Department of Obstetrics and Gynecology Grand Rounds, Georgia Regents University, Augusta, GA, June 2013.

4. *Dichloroacetate Induces Apoptosis of Epithelial Ovarian Cancer Cells Through the Inhibition of Oxidative Stress Enzymes*. SGI-SMFM Scientific Meetings Abstract Presentations, Department of Obstetrics and Gynecology Grand Rounds, Wayne State University School of Medicine, Detroit, MI, February 2010.

5. *PCR Techniques Concepts and Clinical Applications*. Clinical Fellows Seminar, Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, Wayne State University School of Medicine, Detroit, MI, March 2000.

6. *The Role of p53 and Apoptosis in the Pathogenesis of Keloids*. Department of Obstetrics and Gynecology Grand Rounds, Wayne State University School of Medicine, Detroit, MI, July 1998.

Exhibit Y

VITAE

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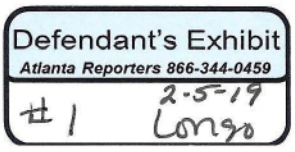
EDUCATION

October 1980 to December 1983	Received Doctor of Philosophy in Materials Science and Engineering, University of Florida
June 1979 to May 1982	Received Master of Science in Materials Science and Engineering, University of Florida.
September 1972 to June 1977	Received Bachelor of Science degree; Major in Microbiology, Minor in Chemistry, University of Florida.

PROFESSIONAL WORK HISTORY

September 1987 to Present	President of MAS, LLC (previously Materials Analytical Services, Inc.) Suwanee, Georgia.
August 1987 to February 1988	President and Founder of Longo Microanalytical Services, Inc., Gainesville, Florida.
October 1983 to August 1987	President and Founder of Micro Analytical Laboratories, Inc., Gainesville, Florida.
March 1985 to December 1987	Visiting Assistant Professor; University of Florida, Department of Materials Science and Engineering.
August 1983 to March 1985	Post Doctoral Associate; University of Florida, Department of Materials Science and Engineering.



PATENTS

U. S. Patent Serial No. 4671954 June 9, 1987. Goldberg, E.P., Iwata, H., and Longo, W.E., "Microspheres for Incorporation of Therapeutic Substances and Methods of Preparation Thereof."

U. S. Patent Serial No. 4871716, October 3, 1989. Goldberg, E.P., Longo, W.E., and McCluskey, R.A., "Magnetically Responsive, Hydrophilic Microspheres for Incorporation of Therapeutic Substances and Methods of Preparation Thereof."

PUBLICATIONS AND PRESENTATIONS

Egilman, D., Longo, W.E., "Egilman's Assessment Regarding Exposures of Auto Mechanics to "Amphiboles is Correct" *Inhalation Toxicology*, 2012: 24(9); 614-618.

Rigler, M.W., Longo, W.E. & Sauerhoff, M.W.: "Exposure to Fluropolymers and VOCs during Spray Sealant Product Use" Inhalation Toxicology, 23 (11): 641-657, 2011.

Ewing, W.M., Hays, S.M., Hatfield, R., Longo, W.E. & Millette, J.R. "Zonolite Attic Insulation Exposure Studies" *Int. J. Occup. Environ. Health*, Vol. 16(3), Jul/Sep, 2010.

Rigler, M.W., Longo, W.E. Emission of Diacetyl (2.3 Butanedione) from Natural Butter, Microwave Popcorn Butter Flavor Powder, Paste, and Liquid Products", *Int. J. Occup. Environ. Health,* 16:291-302, 2010.

Rigler, M.W., Longo, W.E., "Qualitative Sulfur Gas Emission as a Specific Marker for Problematic Reactive Drywall, Proceedings of the Technical Symposium on Imported Corrosive Drywall, November 5-6, 2009, the University of Florida, Gainesville, FL.

Longo, W.E., Rigler, M.W., Russell, P.E., Vitarelli, J.P., Hoffman, E.M. & Johnson, H.M. Health Effects of Welding, "The Characterization of Welding Fume Particulates and Mn Bioavailability Studies for SMAW and FCAW Consumables" NIOSH, West Virginia, July 2005.

Harris M.D., Ewing, W.M., Longo, W.E., DePasquale, C., Mount, M.D., Hatfield, R.L. & Stapleton, R. "Manganese Exposure During Shielded Metal Arc Welding (SMAW) in an Enclosed Space" *J. Occup. & Environ. Hyg.* 2(8) 375-382, 2005.

Longo, W.E., Egeland, W.B., Hatfield, R.L., Stapleton, R., and Hubbard J., "Tremolite Analysis of Chrysotile Containing Friction and Gasket / Packing Products", ASTM Johnson Conference, Johnson Vermont, July, 2002.

Longo, W.E., Egeland, W.B., Hatfield, R.L., and Newton, L.R., "Fiber Release During the Removal of Asbestos-Containing Gaskets: A Work Practice Simulation" *Appl. Occup. Environ. Hyg*. 17(1) 55-62, 2002.

Hatfield, R.L., Krewer, J.A., and Longo, W.E., "A Study of the Reproducibility of the Micro-Vac Technique as a Tool for the Assessment of Surface Contamination in Buildings with Asbestos Containing Materials" (M.E. Beard and H.L. Rook) in *Advances in Environmental Measurement Methods for Asbestos*, ASTM #STP 1342,301, January, 2000.

Rigler, M.W., Freeman, G.B., Longo, W.E., Kyono, M. and Cai, M. "A New Rapid Method for Analyzing Single Particles", Proceedings of the Engineeri9ng Solutions to Indoor Air Quality Symposium for the United States Environmental Protection Agency (USEPA), July 21-26, 1997, Research Triangle Park, NC.

Longo, W.E., and Rigler, M.W., "Rapid Identification of Inorganic and Organic Particulate for Routine IAQ Assessment" Indoor Environment Meeting, April, 1996.

Longo, W.E., "Malignant Mesothelioma in Kent Cigarettes Smokers: Analysis of Asbestos Content in Filters, Cigarette Smoke and Lung Tissue" Society for Ultrastructural Pathology, March, 1996.

Longo, W.E., "The Identification of Asbestos Containing Surface Treatment Products using Standard Analytical Techniques" Florida Environmental and Asbestos Council Meeting, January, 1996.

Longo, W.E., Rigler, M.W. and Slade, J., "Crocidolite Asbestos Fibers in Smoke from Original Kent Cigarettes" Cancer Research 55 11, 2232, 1995.

Longo, W.E., "Occupational Exposure From In-Place Asbestos Containing Fireproofing" Environmental Information Association, April, 1995.

Keyes, D. L., Ewing, W. M., Hays, S. M., Longo, W. E. and Millette, J.R., "Baseline Studies of Asbestos Exposure During Operations and Maintenance Activities" Appl. Occup. Environ. Hyg. 9(11) Nov, 1994.

Goldberg, E.P., Quigg, J., Sitren, H., Hoffmann, E., Jayakrishnan, A., Longo, W. and Cantrell, J., "Microsphere Drug Carriers for Targeted Chemo Immunotherapy and for Intracellular Infections" 20th Annual Meeting of the Society for Biomaterials, 1994.

Millette, J.R., Longo, W.E. and Hubbard, J.L., "Demonstration of the Capability of Asbestos Analysis by Transmission Electron Microscopy in the 1960's" Microscope, 41 15, 1993.

Ewing, W. M., Chesson, J., Dawson, T. A., Ewing, E. M., Hatfield, R. L., Hays, S. M., Keyes, D. L., Longo, W. E., Millette, J. R., and Spain, W. H. "Asbestos Exposure During and Following Cable Installation in the Vicinity of Fireproofing" Environmental Choices Technical Supplement, Volume I, (2), 1993.

Longo, W. E., "Sampling and Analysis of Asbestos in Dust: An Update" Environmental Information Association, April, 1993. Nashville, Tennessee.

Keyes, D. L., Chessan, J., Hayes, S. M., Hatfield, R. L., Ewing, W. M., Longo, W. E. and Millette, J. R. "Re-Entrainment of Asbestos from Dust in a Building with Acoustical Plaster" Environmental Choice, Technical Support, Volume I, (6), 1992.

Longo, W. E. "A Standard Method for the Analysis of Asbestos in Settled Dust by TEM" Asbestos Measurement Risk Assessment and Laboratory Accreditation, ASTM Conference, July 1992. Johnson, Vermont.

Longo, W. E. and Roggli, V. L., "Mineral Fiber Content of Lung Tissue in Patients with Environmental Exposures: Household Contacts vs. Building Occupants" (B. Boland and J. Cullian EDS) in The Third Wave of Asbestos Exposure to Asbestos in Place. *Annals of The New York Academy of Sciences*, Volume 63, 1991.

Keyes, D. L., Chessan, J., Ewing, W. M., Faas, J. C., Hatfield, R. L., Hayes, S. M., Longo, W. E. and Millette, J. R. "Exposure to Airborne Asbestos Associated with Simulated Cable Installation Above and Suspended Ceiling" *Am. Ind. Hyg. Assoc. J.* (52) Nov. 1991

Longo, W. E. "Sampling and Analysis of Asbestos in Settled Dust" EPA/A&WMA Symposium on "Measurement of Toxic and Related Air Pollutants", May 1991. Durham, North Carolina.

Longo, W. E. "Asbestos Wipe Sampling" Industrial Hygiene Association, October, 1990. West Palm Beach, Florida.

Longo, W. E. "Standard Test Method for Asbestos Concentrations in Dust Samples" American Society of Testing Materials Subcommittee D22.05.07, manuscript in progress.

Goldberg, E. P., Yalon, M., and Longo, W. E. "Low Voltage SEM for Unique Surface Analysis of Prosthetic Devices" Materials Research Society Symposium Proceedings 110, *Biomedical Materials and Devices,* 1989.

Longo, W. E. "Field Emission Scanning Electron Microscopy: An Alternative Technique for the Analysis of Asbestos Air Filter Samples" National Asbestos Council, September 1988. Boston, Massachusetts.

Goldberg, E. P., Yalon, M., and Longo, W. E. "Low Voltage Scanning Electron Microscopy for Improved Surface Characterization of Ocular Implants and Other Prosthetic Devices" American Chemical Society Symposium, September 1988. Los Angeles, California.

Longo, W. E. "Rinse Technique for Recovery of Air Samples for TEM Analysis" Asbestos Measurement Research and Laboratory Accreditation, ASTM Conference, July 1988. Johnson, Vermont.

Longo, W. E. "The Presence of Inorganic Fibers in Commercial Brands of Cigarettes" American Industrial Hygiene Conference, May 1988. San Francisco, California.

Longo, W. E. "Analysis of Asbestos by Transmission Electron Microscopy" Alabama Electron Microscopy Society 7th Annual Meeting, March 1988. Birmingham, Alabama.

Longo, W. E. "Asbestos Fiber Loss from Air Sampling Cassettes: A Study by Transmission Electron Microscopy" EPA/APCA Symposium on Measurement of Toxic and Related Air Pollutants, May 1987. Research Triangle Park, North Carolina.

Longo, W. E. "Asbestos Air Sample Analysis by Transmission Electron Microscopy" American Industrial Hygiene Conference Professional Development Course, May 1987. Montreal, Canada.

Longo, W. E., Jenkins, E. J., Greene, R., and Baxter, D. "Water Refiltration: An Alternative Sample Preparation Method for the Analysis of Airborne Asbestos by TEM" National Asbestos Council, January, 1987, Chicago, Illinois.

Longo, W. E., and Goldberg, E. P. in "Drug and Enzyme Targeting" (K. Widder and R. Green Eds) Methods of Enzymology, 112, 18, 1985.

Goldberg, E. P., Iwata, H., and Longo, W. E. "Hydrophilic Albumin and Dextran Ion-Exchange Microspheres for Localized Chemotherapy" (S. Davis, L. Illium, J. McVie, and E. Tomlinson Eds) in Microspheres and Drug Therapy. Pharmaceutical Immunological and Medical Aspects, 10, 309, 1984.

Hoffmann, E. M., Longo, W. E., and Goldberg, E. P. "Macrophage Uptake of Albumin Microsphere Drug Carriers" Proceedings of the 11th International Symposium on Controlled Release of Bioactive Materials, 11, 27, 1984.

Longo, W.E., "Albumin Microspheres for the Controlled Release of Therapeutic Agents" Doctor of Philosophy Dissertation, University of Florida, 1983.

Longo, W. E., and Goldberg, E. P. "Novel Albumin-Polypeptide-Drug Microspheres: Synthesis and Ion Exchange Drug Release Properties" Proceedings of the 10th International Symposium on Controlled Release of Bioactive Materials, 10, 245, 1983.

Longo, W. E., Iwata, H., Lindheimer, T., and Goldberg, E. P. "Preparation and Drug Release Properties of Albumin-Polyglutamic Acid-Adriamycin Microspheres" American Chemical Society, 24, 56, 1983.

Longo, W. E., Iwata, H., Lindheimer, T., and Goldberg, E. P. "Preparation of Hydrophilic Albumin Microspheres Using Polymeric Dispersing Agents" *J. Pharm. Sci.*, 71, 1323, 1982.

Goldberg, E. P., Iwata, H., Terry, R. W., Longo, W. E., Levy, M., and Cantrell, J. L. in "Affinity Chromatography and Related Techniques" (Visser, Visser and Nivard Eds), Elsevier, Amsterdam, 375, 1982.

Longo, W. E., Iwata, H., and Goldberg, E. P. "Hydrophilic Albumin-Polyglutamic Acid-Adriamycin Microspheres for Localized Chemotherapy" 8th Annual Meeting of the Society of Biomaterials, 10, 60, 1982.

ACTIVITIES AND ORGANIZATIONS

* Member of Environmental Protection Agency Workshop on Sampling and Analysis of Asbestos in Settled Dusts, July 1989.

* Member of Environmental Protection Agency Peer Review Group for the Asbestos Engineering Program, 1987 to present.

* Vice-Chairman of the National Asbestos Council Analytical Subcommittee on Transmission Electron Microscopy 1987-1988.

* Chairman of National Asbestos Council Analytical Subcommittee on Transmission Electron Microscopy 1988-1989.

* Member of ASTM D-22-05 Subcommittee for Indoor Air Pollution.

LECTURES AND COURSES INSTRUCTED

Longo, W.E. "Electron Microscopy for Industrial Hygiene Applications" American Industrial Hygiene Conference Professional Development Course, Atlanta GA, May 2004.

Longo, W. E. "Settled Dust: Asbestos and Other Particulates"
Georgia Institute of Technology Seminar, August 1991.

Longo, W. E. "The Role of the Laboratory Manager, Quality Assurance Officer and the Analyst for NIST Accreditation" Georgia Institute of Technology, Transmission Electron Microscopy Asbestos Accreditation Seminar, August 1989.

Longo, W. E. 24th Annual Meeting of the Microbeam Analysis Society,
"Asbestos Analysis Session" Ashville, North Carolina, July 1989 (Session Co-Chairman).

Longo, W. E. "Fundamentals of Asbestos Analysis by TEM" Institute in Materials Science State University of New York. New Paltz, New York, October 1988 (Course Director).

Longo, W. E. "TEM Imaging/Photography" Georgia Institute of Technology, Transmission Electron Microscopy Asbestos Analysis Course, June 1988.

Longo, W. E. "Laboratory Preparation of Polycarbonate Filters for TEM Analysis"
Georgia Institute of Technology, Advanced Transmission Electron Microscopy Asbestos Analysis Course, February 1988.

Longo, W. E. "Transmission Electron Microscopy Laboratory Set-Up" Georgia Institute of Technology, Advanced Transmission Electron Microscopy Asbestos Analysis Course, February 1988.

Longo, W. E. "Laboratory Analysis of Asbestos" Hall-Kimbrell Seminar in Asbestos Abatement in the State of Florida, January 1988.

Longo, W. E. "Air Sample Preparation and Analysis by TEM" Georgia Institute of Technology, Clearance Testing for Asbestos: AHERA Regulations, October 1987.

Longo, W. E. "Asbestos Air Sample Analysis by Transmission Electron Microscopy"
American Industrial Hygiene Conference Professional Development Course, Montreal, Canada, May 1987.

Longo, W.E. "Asbestos Air Sample Analysis by Transmission Electron Microscopy"
American Industrial Hygiene Conference Professional Development Course, Dallas, TX May 1986.

PROFESSIONAL MEMBERSHIPS

American Industrial Hygiene Association	1985 to Present
American Society for the Testing of Materials	1987 to Present
American Society of Materials	1994 to Present
National Asbestos Council	1984 to 1993
Environmental Information Association	1993 to Present
Materials Research Society	1988 to Present
Electron Microscopy Society Association	1988 to Present
Microbeam Analysis Society	1988 to Present
New York Academy of Science	1985 to 1987 1989 to 1994
Air Pollution Control Association	1985 to 1987
National Institute of Building Sciences	1991 to Present
The Society for Ultrastructural Pathology	1996 to Present
American Society of Heating, Refrigerating and Air-Conditioning Engineers	1996 to Present
The American College of Forensic Examiners – Fellow of Forensic Engineering Technology (IN. 17825)	1999 to Present
American Conference of Governmental Industrial Hygienist (ACGIH) Associate Member	2006 to Present

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